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ON THE MECHANISM OF SHOCK OR GENERAL REACTION OF CELLS AND ORGANISMS TO INJURY[1]

(Outline of a Working Hypothesis)[2]

by

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The difficulties involved in a detailed analysis of the mechanism of cell injury may hardly assert themselves more strongly than in the branch of functional pathology that deals with the effect of radiation on the cell.

Owing to the discontinuous quantum nature of radiation, the primary changes will appear at random in the irradiated matter. Penetrating radiation affects all elements of the cell — substances being destroyed and new ones arising in a chaotic manner. Nevertheless, the living cells show merely a limited number of reactions, which do *not* differ from those induced by other »noxious» agencies.

The reaction of cells to injury is *specific* — *i. e.*, depending more or less on the character of the injurious agent — as well as *non-specific* or alike to all agents. The object of the present working hypothesis is merely the unspecific or general reaction of cells to injury. Any change in the surroundings of the cell acts as an irritant, but the injury to the cell does not commence till the irritant attains a certain potency. As the threshold value for the irritant naturally depends on the state of the cell at the given moment, the mechanism of the injury to the cell can

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[2] The studies here presented are carried out with financial support from a private circle.

be realized only on the background of the cooperation of the cell with other cells and organs. This interaction depends on the very phenomena of »irritation» and »reaction», as the cell is not merely susceptible to humoral and nervous impulses but is in itself a starting-point of such.

Most animal cells have no membrane proper, but this want is met by the border layer of the cell or ectoplasm, which deviates more or less from the endoplasm. As all exchange of substances between the cell and its surroundings takes place through the border layer of the cell, the permeability of this is of decisive importance (Fig. 1 a). Selective per-

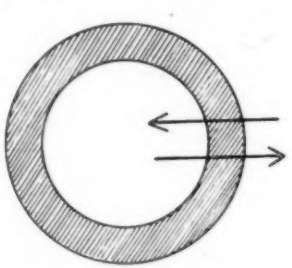

Fig. 1 a.

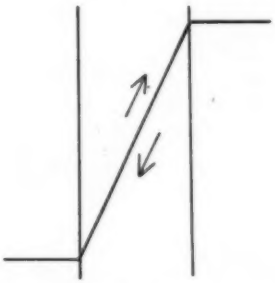

Fig. 1 b.

Fig. 1 a. Exchange of substances through the border layer of the cell.
Fig. 1 b. Fall in concentration of substances in the border layer of the cell.

meability is characteristic of living cells in contrast to dead ones, which are completely permeable. The energy required for the active transport of substances — secretion and absorption — proceeding from lower to higher concentration, is covered by the metabolic processes of the cell. The active transport of substances is counteracted by passive processes of diffusion, proceeding from higher to lower concentration (Fig. 1 b).

In the chemical system of the cell which thus may be designated as »open», false equilibria or »steady states» will be established when the afflux and efflux of substances are equal. In contrast to »closed» chemical systems in which the amounts of substances are constant and in which the equilibria are genuine or stable, the open systems are able to take up and give off energy (Figs. 2 a and b).

Only when the permeability of the border layer of the cell is able to adjust itself to the immediate functional condition of the cell can it act as regulator of the vital processes that manifest themselves, among others, in the aforementioned transport of substances. When a disturbance in the chemical system of the cell is not all too radical — as,

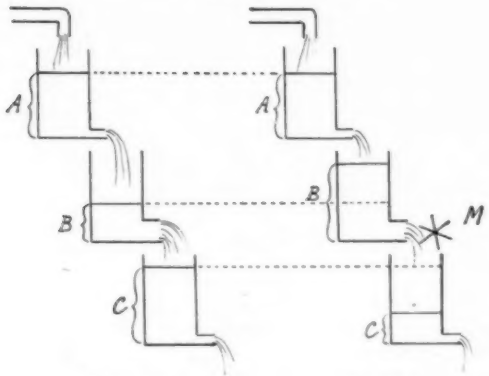

Fig. 2 a. Fig. 2 b.

Fig. 2 a. Stationary state (afflux = efflux).
Fig. 2 b. New stationary state in consumption of energy.

»Open» chemical system of the cell, hydrodynamic analogy illustrating the successive transformation of substances A, B and C.

$$\longrightarrow A \longrightarrow B \longrightarrow C \longrightarrow$$

M represents a water-wheel that delays the stream of water from B to C. The amount of A is unchanged, B increased, and C decreased in relation to the state in 2 a. The amount of substance is indicated by the height of the fluid. Note the differences in the width of the spouts.

for instance, increased dissimilation — the assimilation increases until a new stationary state is attained. In other words, the system develops counterforces against the disturbance, and this adjustment is the cause of the »self-regulatory» character of the system.

As first pointed out by HERING the phenomena of irritation have to be interpreted as reversible disturbances in the steady state of the cells (Fig. 3). As a matter of fact they involve a general principle of biologic functions. The appearance of sensitive substances — *e. g.* visual purple — through the action of irritant and their subsequent elimination bring the phenomena of irritation quantitative to be reckoned under chemical kinetics.

For orientation as to the way in which the cell is influenced, it will be appropriate here briefly to sketch a couple of the main principles of the pharmacological effect: »competitive action» and »potential action».

Numerous drugs exert their effect by competitive action — or, by occupying in competition with other agents, the prosthetic groups of cell surfaces or enzymes (Fig. 4 a—d).

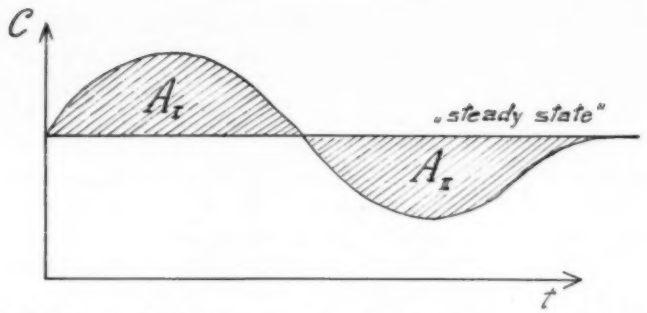

Fig. 3. The irritation phenomenon as a reversible disturbance in the steady state of the cell.
Ordinate: C, concentration of sensitive substance — *e. g.*, visual purple. Abscissa: t, time. $Area_I = area_{II}$.

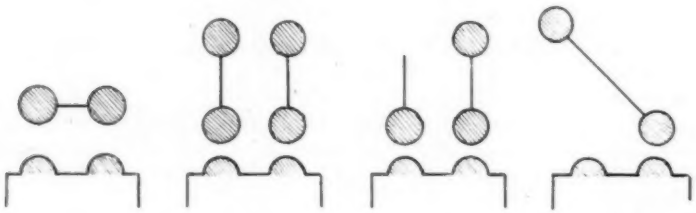

Fig. 4 a—d. »Competitive action», competitive occupation of the prosthetic groups of a cell surface or an enzyme.
Example: Histaminase or diaminoxidase (ZELLER), which possesses 2 active groups that will have to be occupied simultaneously if any effect is to appear.

In contrast hereto, the effect of the so-called »potential substances» (»Potentialstoffe» STRAUB, GREMELS, KAHLSON) is inextricably associated with a fall in concentration directed towards the middle of the cell, with an abruptness that governs the intensity of the effect (Fig. 5 a—d). The action, which lasts only as long as there is a concentration gradient, is elicited by change in the permeability due to the »chemical polarization» of the border layer of the cell. It is characteristic that the effect of potential substances depends on the rate of their supply (time factor).

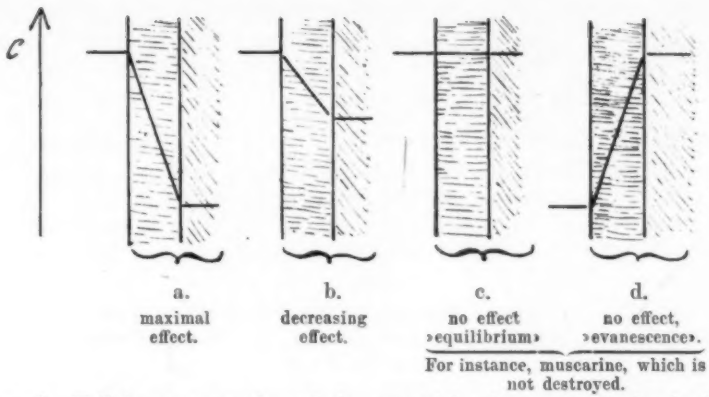

Fig. 5 a—d. Fall in concentration of the potential substance in the border layer of the cell.

Potential substances are: 1) chemical transmitters of the nervous system, adrenaline (sympathetic system) and acetylcholine (vagus, motor nerves); 2) various hormones, vasopressin, insulin; 3) some pharmacologically very active substances, including histamine and perhaps several diamines.

The action of the potential substances is modified by the so-called »conditional substances» (GREMEL's »Zustandsstoffe»), which a) affect the permeability of the border layer of the cell or b) alter the activity of the enzymes which break down the potential substances, or c) both.

a. On increase or decrease in the permeability of the border layer of the cell the fall in the concentration of the potential substance becomes respectively more flat or more abrupt. Atropine and digitalis glycosides, being conditional substances for acetylcholine, will intensify its effect when the permeability of the border layer is lowered.

b. The activity of the enzyme that breaks down a given potential substance determines the »vacuum» of the cell for this substance: increase and decrease in the enzyme activity will respectively promote and retard the fall in the concentration of the substance. Potential substances that are not destroyed in the cell — *e. g.*, muscarine — present the peculiar phenomenon, that their effect ceases when the cell is saturated with them. Only potential substances that are destroyed in the cell are able to produce a permanent effect — a »tonus». Ephedrine lowers the adrenaline-splitting aminooxydase. Physostigmine and prostigmine, which both have the character of urethanes, lower the activity of cholinesterase, which eliminates acetylcholine.

c. »Narcotics», including urethane, have a twofold activity, and the same applies to urea, the end-product of proteolysis. Radiation energy, I think, acts in a similar way, altering the permeability of the border layer of the cell as well as the acting conditions for the enzymes.

As the conditional substances often have points of attack in common, it is easy to understand that synergism as well as antagonism may occur. Thus urea counteracts low concentrations of narcotics, and promotes the effect of the digitalis glycosides. High urethane concentrations promote a general effect of roentgen radiation, both inducing a protracted state of shock.[1]

Generally the electrolytes are reckoned neither as potential substances nor as conditional substances. In my opinion, however, the ammonium ion occupies a special position by itself in this respect. Further, a special rôle as »conditional substances» has to be assigned also to ammonia, amines, polypeptides and nucleic acid compounds in the general reaction of the cells and the organism to injury (see below).

Whenever living cells are exposed to the action of various agencies, the starting point for the biological effect is to be looked for in the attack on the molecules of the cell. But, as molecules belonging to the structure of the cell at a given moment may merely constitute metabolic products at the next instant, no sharp border line can be maintained between the molecular anatomy and physiology of the cell. In brief, the walls of the

[1] Three years ago I first observed this synergism between urethane and roentgen radiation, while I was carrying out some experiments on guinea-pigs in which it was essential that the animals did not move during the irradiation. Both the considerable doses of urethane and the doses of roentgen rays here employed, applied to the back (abdomen) — were separately tolerated well, but many of the narcotized and irradiated animals died.

In a previous monograph by Scott (»Quantitative aspects of the biological actions of X- and γ-rays», Medical Research Council, 1937) I had read that the radiation effect on blow-fly eggs could be accentuated by anesthetics (chloroform, ether and petroleum ether, but *not* by nitrous oxide).

Now with the aid of a grant from the National Association for Cancer Control I commenced some extensive quantitative experiments on mice in order to study the lethality of the combination of urethane and radiation. These experiments were being carried out in the Laboratory of the Radium Station — but I had to leave this laboratory and thus interrupt the experiments.

Besides, theoretical considerations let me on to the treatment of roentgen-ray intoxication with adrenal cortical hormone.

In the autumn 1944 I gave some lectures on »Biological Aspects of Radiotherapy». Notwithstanding the observations above, on this occasion my statement about some chemical substances being able to accentuate, others to attenuate, the radiation effect was met with skepsis.

vessel participate in the chemical processes of its content — just as in chain reactions of gases.

All agencies acting on the cell will alter the synthesis and cleavage of the cell proteins and thus also the other metabolic processes in the cell, as they indeed are governed by the varying catalytic properties of the protein structure.[1]

The fantastic dynamics of the cell-structure is due to the particular molecular combinations or symplexes (WILLSTÄTTER, PRZYLECKI) into which protein enters with inorganic as well as organic cell elements, producing the space- and time-relation of the molecules which caracterizes the living cell. The time-connection of the molecules is disclosed characteristically in the hysteresis of many cellular phenomena — a lagging or »remembrance of previous states gone through» — a striking example of which is found in the time-factor of the radiation effect. Hormones and vitamins which are closely related to the enzymes, appear to be able to exert their activity only in connection with colloid structures (EULER). The enzymes are already symplexes, consisting of a prosthetic group and a colloid carrier.

The general reaction of the cells to injury is dominated by two phenomena, which both correspond to an accentuated physiological strain, namely:

A. Inhibition or paralysis of the Pasteur mechanism.
B. Disturbance of the osmoregulation.

The Pasteur mechanism — or the resynthesis of lactic acid to glycogen — is directly connected with the protein structure. Injury gives accumulation of lactic acid, reduction in the alkali reserve and transitory increase in the carbon dioxide output. The Pasteur mechanism is affected by a number of nitrogen compounds.

Even physiological cellular activity is associated with liberation of ammonia, amines, polypeptides and adenosin compounds, which dif-

[1] The processes catalyzed by the protein structure chiefly involve oxidation-reduction and hydrolytic condensation.

In the first-mentioned processes the transmission of electrons is associated with the prosthetic groups of special enzymes, the colloid carrier of which exerts a similar influence as does the rest of a dye molecule on the chromophoric group of the molecule.

In the hydrolytic cleavage of ester compounds due to acid-base catalysis (BRØNSTED) the circle of the proton transmission is completed through the molecules of the colloid structure that take up and give off protons under shifts in the electronic structure.

On the whole, molecules and atomic groups with quantum-mechanic resonance play a prominent rôle in numerous cellular phenomena. For instance, carbonyl groups are of great importance in several enzymes — *e. g.*, diaminoxydase and histidine-decarboxylase. Carbonyl groups play an important rôle in the phosphorylation of many substances.

fuse readily and exert their influence on the protoplasm, border layer of the cell, endothelium and smooth musculature. The affect is due to the swelling increase in the biocolloid through mechanisms in which the quantum-mechanic resonance presumably plays a rôle.

When present merely in relatively slight amounts, the nitrogen compounds stimulate the protein synthesis and the growth of the cells, so that the normal wear of the tissue cells is repaired. Amines, ammonia and polypeptides increase the permeability of the capillaries; amines and ammonia induce also capillary dilatation with reactive hyperemia (congestion) thus promoting the exchange of substances.

When, through pathological cell activity or injury, these substances appear in relatively large amounts, they exert a deleterious effect on cells and membranes, introducing a state of shock. Ammonia, amines and polypeptides increase the permeability of the border layer of the cell and the hydration of the protoplasm excessively. Under this hydration, which is promoted by the presence of lactic acid and other low-molecular products, the cells swell, the cytoplasm becoming opaque owing to protein precipitation, the »cloudy swelling» of the pathologist. The permeability of the endothelia increases to such an extent that albumins pass through; and the capillary dilatation reaches such degree that stasis with stagnation of the erythrocytes results (hemoglobin being kept from circulating).

If the abnormal hydration of the cellular structures keeps increasing, the energy production of the cells will finally be paralyzed, so that all synthesis and active transport of substances — absorption and secretion — ceases. The continued passive processes of diffusion gradually bring about a balance of substances between the intracellular and extracellular spaces, causing characteristic shifts of electrolytes: potassium leaving the cells, sodium entering, etc. Even physiological irritation liberates potassium from the cells.

The abnormal permeability of the capillaries and the absorption of water by the tissues result in hemoconcentration (increasing hematocrit value), decrease in the amount of circulating blood, tissue anoxia with abnormal metabolism of the cells and new deleterious conditions affecting the cells and endothelia, *i. e.*, the vicious circle leading on to shock of the total organism.[1] Whether this turns out to be acute or protracted will depend on the extent to which the organism is able to mobilize counter-regulatory measures. Striking examples of protracted states of shock are found in roentgen intoxication and toxemia of pregnancy.

The state of shock is counter-acted by desoxycorticosterone, adrenocortical hormone, which stimulates the cellular synthesis of protein, thus tending to normalize the injured protein structure of the cells. The hor-

[1] The interruption of the osmoregulation of the cells is designated by the writer as »cell shock».

mone is not likely to have any direct affect on the important processes of phosphorylation, which depend on the optimal hydration of the protein structure. As is well-known, sodium chloride alleviates adrenal cortical insufficiency. Through the symplex formation with enzymes the cortical hormone will block the metabolism of certain phosphate compounds.[1]

It is reasonable to assume that vasopressin has an effect antagonistic to desoxycorticosterone — just like other polypeptides — perhaps through the Pasteur mechanism.

Owing to the incapacity of the adrenal cortex for immediate adjustment, acute physiological strain and shock are associated with cortin insufficiency. In protracted shock, on the other hand, the hormone production is increased through hypertrophy of the organ, as the aforementioned nitrogen compounds constitute an adequate stimulus for the adrenal.

The adrenocortical hypertrophy is accompanied by involution of the lymphoid system — the so-called alarm reaction (SELYE). No involution of the lymphoid system takes place in adrenalectomized animals. It seems reasonable to assume that the effect of non-focal roentgen irradiation and urethane on the thymus, spleen and lymph glands is due in part to the alarm reaction, something which — as far as I know — has not been pointed out by ALEXANDER HADDOW & EDITH PATERSON (1946), who discovered the serviceability of urethane as a remedy against leukemia. As also the myeloid leukopoiesis is strongly affected by this treatment, there can be no doubt that the inhibition of certain dehydrases — perhaps especially glutamic acid dehydrase — which reduce cytochromoxidase, plays a rôle in this respect.

Closely related to the adrenocortical hormone is tissue histaminase or diaminoxidase,[2] which, besides histamine, oxidizes most diamines. In

[1] The effect of hexokinase is thus abolished by symplex formation of the enzyme with desoxycorticosterone and a proteose from the hypophysis. The blockade is broken by insulin, as has been demonstrated in vitro by C. F. CORI.

[2] Diamine oxidase is also subject to the action of other hormones. In this way, among others, it seems possible to explain the greatly increased activity of diamine oxidase during pregnancy (ZELLER), in which a new hormone-producing organ — the placenta — is added to the mother organism. Very likely, a primary causal rôle in toxemia of pregnancy is to be assigned to the shift in the estrin-prolan balance resulting from the abnormal prolan output of the placenta during this condition (SMITH & SMITH). Also estrin has a certain effect on toxemia of pregnancy. The similarity between menstrual oedema and toxemic oedema is hardly accidental — a feature characteristic in this respect being the low estrin content of the urine just before the menses. Undoubtedly the pituitary dysfunction of toxemic and ecclamptic patients with increased vasopressin production (ANSELMINO & HOFFMANN) is a secondary phenomenon induced by the placental prolan.

states of shock, in spite of the increase in its activity, this enzyme is not able to cope with the overwhelming amounts of amines. Through »competitive action» with acetylcholine the diamines block the action of choline esterase, the substrate split product of which, choline, otherwise inhibits diamine oxidase. Thus the activity of choline esterase is lowered, so that the action of acetylcholine is prolonged, giving rise to the vagotonus that characterizes many of the clinical symptoms in shock.

Most likely, it will be correct to assume that the nitrogen compounds mentioned repeatedly in the preceding correspond to the »adrenal insufficiency substance» of RIML that can be demonstrated by injection of blood dialysate into guinea-pigs. The occurrence of toxic substances in the blood of animals exposed to roentgen-irradiation has been demonstrated previously in parabiosis experiments. It is rather probable that also a »toxemic toxin» may be demonstrated by employment of RIML's technique.

Finally, mention is to be made of the »adaptation function» (SELYE) of the adrenal cortex in muscular work (training), repeated injections of histamine (desensitization) and ultra-violet light irradiation (J. E. Th.). The adaptation is due to hypertrophy of the adrenal cortex induced by the nitrogenous substances produced or supplied for a considerable length of time.

Injection of histamine stimulates the hormone output of the adrenal cortex (and of the medulla too), and thus it is able to replace parenteral administration of adrenocortical hormone. So, after the present working hypothesis it should be possible to treat roentgen intoxication with sodium chloride, adrenocortical hormone and histamine. The employment of sodium chloride — a diet rich in salt, intake of salt tablets — is based on old experiences. The writer preferably employs desoxycorticosterone acetate in sesam oil, given intramuscularly (percorten, Ciba), for instance, 10 mg half an hour before irradiation. The histamine effect predicted by this hypothesis has been confirmed by S. KULLANDER (in a paper read at the 13th meeting of the Scandinavian Society of Medical Radiology, in Copenhagen, on June 14, 1946).

Conclusions

The mechanism of the general reaction of cells and organisms to injury is elucidated through a working hypothesis taking into account the interaction between the affected cells and other cells and organs.

1. Living cells show only a limited number of reactions to injury.

2. The definition of the phenomenon of irritation as a reversible disturbance in the »steady state» of the cell is amplified into a principle of general validity for biological functions.

3. On the basis of the main principles of pharmacological activity, »competitive action» and »potential action», the origin of the phenomenon of irritation is outlined. Mention is made of »potential substances» and »conditional substances».

4. Radiation energy (and urethane) has a similar action as the conditional substances, the permeability of the border layer of the cell being altered — as well as the conditions for the activity of the enzymes splitting the potential substances. The synergism observed between roentgen radiation and urethane is mentioned in passing.

5. The difference between »irritation» and »injury» is merely quantitative.

6. The non-specific injury to the cell manifests itself in:

a) Transitory increase in the carbon dioxide output (more or less complete inhibition of the Pasteur mechanism, accumulation of lactic acid, decrease in alkali reserve);

b) disturbance of the osmoregulation (complete permeability, stop of the energy production, cessation of synthesis and active transport of substances, balance of intracellular and extracellular elements through diffusion); and

c) emission of nervous and humoral impulses (liberation of nitrogen-containing substances, antagonism between histaminase (diamine oxidase) and cholinesterase, vagotony).

The central point in the mechanism of the injury is the change in the protein structure of the cell that governs the chemical exchanges of the cell.

7. Ammonia, amines, polypeptides and adenosin compounds that are liberated from the cells by physiological strain as well as by pathological cell activity or injury are assigned a particular significance as to regeneration of the tissues and the general effect on the organism produced by the local injury.

8. The function of the adrenal cortex is determining for the defensive capacity of the organism, as desoxycorticosterone stimulates the synthesis of protein by the cells and thus tends to normalize the injured protein structure. The aforementioned nitrogen compounds constitute an adequate stimulus for the adrenal cortex.

Acute states of shock are associated with cortin deficiency or relative adrenocortical insufficiency on account of the incapacity of the organ for immediate adjustment to the increased requirement. In protracted states of shock an adaptation takes place, the adrenal cortex undergoing functional hypertrophy.

9. The involution of the lymphoid system, thymus, spleen and lymph glands accompanying the adrenocortical hypertrophy (SELYE's

alarm reaction) explains in part the effect of roentgen radiation and urethane in leukemia.

10. Roentgen intoxication as well as toxemia of pregnancy represent protracted states of shock, which, according to the theory and experiments presented by the writer, are amenable to treatment with desoxycortisosterone. Histamine, which stimulates the hormonal output of the adrenal cortex, may be employed instead — something that has been confirmed as far as roentgen intoxication is concerned by S. KULLANDER. No experiences are yet available as to the effect of histamine injection in toxemia of pregnancy.

11. The susceptibility of the amine metabolism and nervous processes to radiation is taken to be of significance to the treatment of many lesions — *e. g.* arterial hypertension and bronchial asthma.

Both in essential hypertension and in toxemia of pregnancy (in the pre-ecclamptic stage) irradiation of the hypophysis should be tried — because of the interaction between hormones and amine-splitting enzymes. The writer's material of roentgen-treated hypertonics is still too small for publication.

It is the hope of the writer that this contribution will help to underline the necessity of the establishment of adequate radiobiological laboratories in all countries where roentgen rays are employed in the treatment of disease.

I wish to express my sincere thanks to the private circle —represented by Mr. I. C. MØLLER, Director of »Cold Stores» and Mr. EJVIND MØLLER, Supreme Court Counsel, for its understanding and generous aid.

Finally I wish to thank Professor K. LINDERSTRØM-LANG, Director of the Chemical Department of the Carlsberg Laboratory for his kindness in reading the manuscript of this paper and discuss it with me.

As to a more detailed account of the working hypothesis here presented, the reader is referred to a monograph, now in preparation, and subsequent papers.

The following papers, based on this hypothesis, have appeared:

1. J. E. THYGESEN & E. MØLLER-CHRISTENSEN: Fractional serum protein analysis by means of hypobromite titration. Acta medica Scandinav *125*, 538, 1946.
2. J. E. THYGESEN & E. MØLLER-CHRISTENSEN: Nogle Betragtninger vedrørende Shockproblemet og Desoxycorticosteronets Virkemaade. Nordisk Medicin *31*, 2195, 1946.
3. E. MØLLER-CHRISTENSEN & J. E. THYGESEN: Investigation of the serum protein balance in normal and toxaemic pregnant women. Journ. Obstetr. a. Gynecol. (British) *53*, 327, 1946.

SUMMARY

According to the working hypothesis outlined here, the general as well as the local defence of the organism is closely associated with the amine metabolism and vegetative nerve processes.

No matter whether a local injury to the tissues of the organism is produced by morbid processes or by intentional measures (*e. g.* roentgen radiation) a general effect will appear, threatening the existence of the organism. This reaction is connected, among other things, with the processes of regeneration, by which the organism tries to counteract the local necrobiosis.

Without a fairly thorough knowledge of the mechanism in the non-specific reaction of the cells and organism to injury, neither the radiotherapy hitherto employed nor the possibilities implied in the employment of atomic energy in the control of cancer can be fully utilized.

ZUSAMMENFASSUNG

Der hier skizzierten Arbeitshypothese nach, hängt sowohl die allgemeine als auch die lokale Abwehr des Körpers eng mit dem Aminumsatz und den Vorgängen im vegetativen Nervensystem zusammen.

Gleichviel ob eine lokale Schädigung der Gewebe des Körpers durch krankhafte Vorgänge oder durch absichtliche Massnahmen (z. B. Röntgenbestrahlung) verursacht ist, so wird eine allgemeine und lebensbedrohliche Wirkung eintreten. Diese Reaktion hängt u. a. mit den Regenerationsvorgängen zusammen, durch die der Körper der lokalen Nekrobiose entgegenzuwirken versucht.

Ohne einigermassen eingehende Kenntnis des Mechanismus' der unspezifischen Reaktionen der Zellen und des Körpers auf Schädigungen, können weder die bisher verwendete Radiotherapie noch die der Verwendung der Atomenergie zugeschriebenen Möglichkeiten zur Bekämpfung des Krebses voll ausgenutzt werden.

RÉSUMÉ

Selon l'hypothèse de travail esquissée ici les défenses de l'organisme, tant générales que locales, sont en étroite corrélation avec le métabolisme aminé et les processus nerveux végétatifs.

Peu importe que la lésion locale des tissus de l'organisme soit causée par des processus morbides ou par des mesures prises intentionnellement (par ex. une irradiation aux Rayons de Roentgen), on voit apparaître un effet d'ordre général, menaçant l'existence de l'organisme. Cette réaction est en relation, entre autre, avec les processus de régénération par lesquels l'organisme essaye de contrebalancer la nécrobiose locale.

A défaut d'une connaissance suffisamment approfondie du mécanisme de la réaction non spécifique opposée par les cellules et l'organisme à une lésion, ni la radiothérapie telle qu'on la pratique jusqu'ici, ni les possibilités que recèle l'emploi de l'énergie atomique pour lutter contre le cancer, ne sauraient être utilisées de façon tout à fait complète.

THE TECHNIQUE OF CHEST FLUOROSCOPY [1]

by

L. Walk

Although the diagnostic results in chest fluoroscopy are greatly depending on the technique of the screen exploration, not only on the clinical experience of the roentgenologist, this technique apparently is considered to be simple and has only exceptionally been described in detail. In the following article the author's technique of chest fluoroscopy is described.

Fluoroscopy has to visualize hidden lesions as well as to disclose typical aspects which cannot be found out by means of films made by a technician in some prescribed positions. Extensive use is made of rotating the patient during fluoroscopy, making use of parallaxis in localizing pathological alterations and in dissolving summation artefacts; a three-dimensional conception of the chest is to be obtained. The pulmonary apices are also inspected by altering the position of the shoulder and of the clavicle. Diagnostically valuable aspects found out at fluoroscopy are fixed by means of spot films. Every exploration is completed by a standard roentgenogram of the chest, showing those finer structural alterations which cannot be seen at fluoroscopy.

During the first phase of the exploration (inspection of the diaphragm and the basal parts of the lungs) the patient is asked to breathe deeply; he is rotated first to one and then to the other side, a rotation of 45 degrees being sufficient to see every projection. The patient is hold by his wrists, thus having the possibility to rotate him and at the same time to dislocate his arms if those are in the way in some projection. A medium-sized diaphragm is used; the screen, if coppled to the target, can be moved by the forearms of the roentgenologist, without loosing time by altering the position of his hands. — The second phase (inspection of the heart and the mediastinum and of the general configuration of the chest) is also made with a medium-sized or even wide diaphragm. The technique is the same as during the first phase; in complicated cases it is useful to have the patient his arms elevated, thus having especially suitable con-

[1] Submitted for publication, July 26, 1946.

ditions for examining the chest in every projection. The third phase (inspection of the lungs, especially of the apices) is made with a smaller diaphragm of about 10 × 15 cm or even less (if necessary, its size is varied during exploration). The patient is now hold by his upper arms, the shoulders are pulled down and forward, and going out from this position it is easy to rotate the patient and at the same time to alter the position of the shoulder girdle and thus to see any part of the apex. Beginning with the apex the ray cone is successively drawn downward while continuously altering the patient's position.

If the roentgenologist has once carefully analyzed every detail of the technique, and then has trained all movements carefully, a chest exploration can be performed in ½—2 minutes and only in complicated cases more time is needed. Thus the technique can be maintained even in forced work. If the record is not written immediately after having finished the screen exploration, short personal notes should be made by the roentgenologist, to be used later together with the films. If possible, fluoroscopy is performed with the patient standing, as it is easy to rotate him in this position. I have used 80—95 kV peak and 3 mA in chest fluoroscopy (using a fine lamellar grid), a tension higher than usually mentioned in the literature. If STIEHM states, that two of his hundred patients could not be explored because of great body diameter, this seems to depend on the use of lower tension. I am no more making use of the increasing of the transparency of the pulmonary apices at expectoration; only structural alterations, not vague differences in translucency are of diagnostic value. For the same cause I am examining both lungs separately (thus having the possibility to use a smaller diaphragm), only exceptionally comparing the translucency of both sides.

Although the study of the four standard projections (frontal, lateral, and two oblique projections) is of didactic value, the fluoroscopic technique should not be based on some fixed projections, as it then loses one of its most important properties — finding out optimal aspects.

It has been shown by STIEHM that fluoroscopy is superior to standard films in diagnosing apical tuberculosis; a review of the literature on fluoroscopy, especially in tuberculosis, is found in the monograph of ROSEN. Fluoroscopy is also superior to standard films in detecting pleural fluid, disc-shaped atelectases, various hidden pulmonary affections, and in the differential diagnosis of supraclavicular glandular calcifications and apical calculi.

SUMMARY

It is the technique and not only the clinical experience of the roentgenologist which determines the diagnostic results in chest fluoroscopy.

The author's technique is described.

ZUSAMMENFASSUNG

Das diagnostische Ergebnis der Durchleuchtung der Brustorgane wird durch die Untersuchungstechnik, nicht nur durch die klinische Erfahrung des Untersuchers bestimmt.

Die Technik des Verfassers wird beschrieben.

RÉSUMÉ

Les résultats diagnostiques de la roentgenoscopie des organes intrathoracales ne dépendent pas seulement de l'expérience clinique de l'examinateur, mais aussi de la technique de l'exploration.

Déscription de la technique de l'auteur.

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TRANSPOSITION OF VISCERA — BRONCHIECTASIS AND NASAL POLYPS[1]

A genetical analysis and a contribution to the problem of constitution

by

Johan Torgersen

It has been established that bronchiectasis and nasal polyps occur relatively often in individuals with transposition of viscera. (KARTAGENER, HORLACHER, ADAMS and CHURCHILL, OLSEN, A. M., Mayo Clinic).

In recent years I have collected 129 individuals with situs inversus viscerum in Norway, 123 with complete transposition, partly from clinics, mostly from large series of roentgen examinations in different parts of the country. In a continuous series of 315,336 individuals transposition of viscera was found in 41 cases, approximately 1 : 8,000 corresponding to a total of 350 individuals with the anomaly in the population of Norway. Accordingly my material represents one-third of all individuals with transposition of viscera in this country.

Among 121 families collected at random I found the anomaly in more than one sibling in two cases only. I have examined personally so many of the siblings and their parents as possible. It is rather difficult, however, to carry out a complete investigation in such a large number of individuals, especially taking into consideration the distances in Norway. Supposing recessive inheritance, the greater part of the rest of the individuals with the anomaly in Norway must be concealed among the 573 brothers and sisters of the 123 individuals with transposition of viscera first detected. Such supposition, however, may safely be excluded.

Transposition of viscera in more than one sibling has been reported in Norway on two previous occasions (TH. FRØLICH, H. NATVIG). Two cases of familial transposition in my series of 121 non-selected fraternities would correspond to approximately six such families among

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all fraternities in Norway in which transposition of viscera probably occurs. As it may also reasonably be assumed that such observations would be published, it is highly probable that the cases recorded by FRØLICH, NATVIG and myself, represent all cases of familial transposition of viscera in the population of Norway to-day. Such a calculation makes it improbable that I have overlooked any cases of situs inversus in the fraternities. The possibility that I may have overlooked one or two cases of transposition cannot be ruled out. To a great extent, however, this source of error is compensated for in my including the two cases of familial situs inversus which — having been published previously — must be regarded as selected cases, thus tending to give a higher incidence of familial cases than in a material collected at random.

Among 129 individuals with the anomaly I found bronchiectasis ten times, *i. e.* 8 per cent. Bronchography was performed five times only. OLSEN also has carried out this examination five times in a material from the Mayo Clinic, consisting of 85 cases of dextrocardia, including 14 cases with bronchiectasis. In my material nasal polyps occurred in 11 individuals, *i. e.* 8 per cent. Five of these had bronchiectasis. Thirteen complained of frequent attacks of bronchitis and bronchopneumonia from early childhood. All of these had complete transposition of viscera. OLSEN found that 10 of the 14 patients with bronchiectasis had nasal polyps. Four of the 85 cases with dextrocardia had nasal polyps, and no bronchiectasis. My material, consisting largely of non-clinical cases, indicates that approximately 10 per cent of all individuals with transposition of viscera have symptoms of these lesions of the nose and respiratory tract.

Previous investigators have not attempted to penetrate further into the problem of the causes of this peculiar combination. The solution of the problem depends upon the demonstration of the genetics of the transposition of viscera, of bronchiectasis and nasal polyps and the interplay between the hereditary mechanisms of these two conditions.

COCKAYNE maintains having proved that transposition of viscera depends upon a single autosomal recessive gene. My own analysis, made in the usual way, excluding as selected all the individuals with transposition first detected, does not confirm this result. It is evident that COCKAYNE has not excluded the individuals first detected. The 123 individuals with transposition first detected had 573 brothers and sisters, the anomaly occurring only in six of them. This is a fundamental difference from the ratio of 1 : 3 expected in recessive inheritance.

On the other side consanguineous marriages among the parents are found in 7.3 per cent. Three times they were first cousins, *i. e.* 2.4 per cent, six times second cousins. This incidence of consanguineous marriage is probably somewhat higher than in the population in general, but according to DAHLBERG lower than expected in recessive inheritance of a

character with an incidence of 1 : 10,000. COCKAYNE found that the parents were first cousins six times in 53 families. This comparatively high incidence may be accidental, the number of families being relatively small. It may be doubtful, however, if COCKAYNE's series of families may be regarded as representative. They lived in different parts of the British Empire. It may be of some importance that my material is collected from the relatively homogeneous and small population of Norway. The risk of selection is likely to be smaller in such a material.

The individuals with the anomaly are evenly distributed in the population. They are not accumulated in isolated places where consanguineous marriages are frequent.

COCKAYNE has seen the anomaly twice in uncle and nephew, and he mentions that it is reported to have occurred once in cousins and once in a man and his maternal grandfather.

In mother and daughter it has been reported only once (MATTISON). PERNKOPF observed the anomaly in a father and partial transposition in his child.

Thus the hereditary mechanism of transposition of viscera is a rather tangled problem, a few observations tallying with recessive inheritance, a few with dominant. On the whole the result of the analysis of the relatively large material, however, is not in conformity with a simple mendelian mechanism at all. The possibility remains that transposition of viscera occasionally is inherited as a dominant character, occasionally as a recessive one, and that in many cases the anomaly is not hereditary at all.

Is the genetics of bronchiectasis apt to clear up the problem of the genetics of transposition of viscera? On the other hand, what information does the situs inversus viscerum give about the basis of bronchiectasis and nasal polyps?

According to KARTAGENER bronchiectasis have been reported three times in father and children, and several times in siblings. These few observations may be regarded as indications of dominant inheritance.

The coincidence of bronchiectasis and transposition of viscera in the same family, according to KARTAGENER, has been recorded once in two siblings, with bronchiectasis and situs inversus in both, once in three, with bronchiectasis and nasal polyps in all of them (AREAL LOPEZ). In another case a mother with transposition had a son with bronchiectasis and chronic ethmoiditis (quoted by DIEHL). COCKAYNE reports bronchiectasis and situs inversus in a boy, and in his brother bronchiectasis only. These few observations may be regarded as indications of the familial altneration of bronchiectasis and transposition of viscera.

In order to get a more solid basis for the penetration into this problem I have investigated, on the one side how often these conditions occur in

the siblings and parents in the presence of nasal polyps or bronchiectasis in the individuals with transposition of viscera. On the other side I have endeavoured to discover the incidence of such symptoms in the siblings and parents in families in which the individuals with situs inversus did not suffer from these diseases.

To a great extent such an investigation has to be based on information from the patients, and is not quite exact, therefore. The sources of error however, are uniform in the whole material, which is well suited, therefore, for comparison of the two groups.

The symptoms occurred in 22 families comprising 28 individuals with the anomaly. These 28 individuals had 77 brothers and sisters. A total of 19 of the 77 siblings had symptoms of these diseases in the nose and bronchi. All the other individuals with situs inversus, but without any signs of these morbid conditions, had a total of 496 brothers and sisters, three of whom only had nasal polyps, none bronchiectasis. The difference between the two groups in per cent is $24.66—0.6\ [(19:77) — — (3:496)] = 24.05 \pm 2.24$. Thus, there is a convincing difference between the two groups. The cases of bronchiectasis and nasal polyps are accumulated in the families of the individuals with transposition who suffer from these diseases.

With regard to these diseases the proportion between affected and normal among the 77 siblings is 19: 58. This distribution apparently fits in with the assumption of recessive inheritance in the constitution, which is the basis of these affections of the nose and bronchi.

This assumption, however, does not tally with the distribution of these affections in the parents in the same two groups. The symptoms occurred eight times in 44 parents in the 22 families in which the individuals with situs inversus suffered from these diseases. On the other hand they occurred only twice in the 202 parents in the remaining families. The difference between the two groups is $18.18 — 0.99\ [(8:44) — 2:202)] = = 17.9 \pm 3.3$. Thus, there is also a convincing difference between the parents in the two groups. These affections are more common in the parents of the individuals with situs inversus suffering from nasal polyps and bronchiectasis. In connection with the previous observations this fact makes dominant inheritance highly probable.

According to general clinical experience nasal polyps is an allergic disease. Several of my patients have been examined in the Department of Ear, Nose and Throat Diseases. The assumption of dominant inheritance is in accordance with the experience that allergic conditions in general are inherited as a dominant character with great variations in probability and mode of manifestation.

The parents were not first cousins in any of these families. Once they were second cousins. This may be mere chance.

It is worth noting that the affections of nose and bronchi occurred in all the four familial cases of transposition, and that this was the case also in two of the extremely rare familial cases reported in the literature. The parents are not consanguineous in any of these four families.

In these 22 families the siblings with transposition of viscera first detected, had 6 brothers and sisters with this anomaly and 77 without. The proportion 6 : 77 is also so far from the expected mendelian ratio 1 : 3 that it is not reasonable to assume recessive inheritance of transposition of viscera in these families either.

These facts are not indicative of the dominant gene or genes causing bronchiectasis and nasal polyps, and a recessive gene causing transposition, being linked.

I have not investigated systematically the offspring of the individuals with situs inversus, and my knowledge of the previous generations is fragmentary. One patient told me that her grandfather, but not her parents, had the same affection of the respiratory tract, another that both her father and her paternal grandfather were suffering from these diseases. One of the individuals with transposition with no signs of affection of the nose and bronchi, recounted that his father had been coughing severely with a large quantity of expectorate from the age of 35 to 75. He died »because he had been coughing his lungs to pieces». None of his many children developed any tuberculous disease, a fact which may be interpreted as indicative of his own pulmonary lesion being non-tuberculous. He himself had three children, two of whom with nasal polyps.

In an examination of approximately 70 cases of bronchiectasis ULRICH has found that these patients had rather small frontal sinuses. I have examined the frontal sinuses in individuals with transposition of viscera, among them 14 with symptoms of nasal polyps and bronchiectasis. The material is still too small, and on this occasion, therefore, I shall not go into detail on this subject. My preliminary results support the view of ULRICH that individuals with bronchiectasis have rather small frontal sinuses. On the other hand the frontal sinuses were not underdeveloped in the 23 individuals with transposition of viscera and without nasal polyps and bronchiectasis.

The underdevelopment of the frontal sinuses thus is probably correlated to the affections of the nose and bronchi, not to the transposition of viscera.

The developmental processes underlying the small sinuses may be taken as a parallelism of the genetics of bronchiectasis and transposition of viscera. The constitution of these individuals and the affections of nose and bronchi are genetically independent of the transposition of viscera.

This anomaly is not bound to a particular hereditary mechanism in all cases. The hereditary character in these families is not the anomaly, but the constitution and the predisposition to particular diseases of the nose and bronchi. The remaining individuals with the anomaly, amounting to 90 per cent, have no correlation to these affections and the underlying hereditary mechanism. They represent perhaps several other genetical problems. This explains the contradictory observations of the hereditary mechanism in this anomaly. It may be connected with recessive as well as with dominant genes, in some cases indicating recessive heredity, in others dominant. The fact that the proportion between affected and normal with regard to bronchiectasis and nasal polyps in the siblings in my material, is not in conformity with the expected ratio 1 : 1 in dominant inheritance, may depend upon the probability of manifestation. Not taking this into consideration, the assumption of dominant inheritance of allergy in many cases would be contradictory to clinical experience.

The fact that the symptoms from the respiratory tract were found in the familial cases may perhaps indicate a correlation between probability of manifestation and tendency to transposition. Perhaps the most probable explanation is that bronchiectasis and nasal polyps in individuals with this rare anomaly, are caused by the gene or genes generally underlying the contitutional predisposition to these affections, and that for some reason or other the probability of manifestation is greater in individuals with the anomaly, increasing with the tendency to tranposition. Whether the transposition is complete or not is of no importance.

I cannot agree with COCKAYNE, therefore, when he states that a certain gene is causing transposition, and that this gene sometimes is a disadvantage to the individual. My investigations indicate the reverse: a gene or genes causing bronchiectasis and nasal polyps, may sometimes cause transposition of viscera. This anomaly, therefore, to speak the language of the geneticist, is a result of the pleiotropic action of the genes, or to speak the language of the experimental zoologist, it is the result of the processes and forces in the physiology of development.

It is not justified to assume that the inheritance of constitutional traits is caused by a single gene. One or several genes may play a rôle, acting upon the general balance of the genes. It is well known how another peculiar constitutional trait, the sexual differentiation, depends upon the general balance of the chromosomes. The hereditary mechanism in anomalies of sexual differentiation indicates that a single gene may be sufficient to disturb this balance, and in subsequent development the hormonal balance. According to KARTAGENER bronchiectasis have been reported in some cases of anomalies in somatic sexual differentiation. This may be more than a mere accident.

It is probable that the variations in the manifestations of bronchiectasis and nasal polyps may depend upon the interplay of several genes. The transposition discloses another factor of importance. The bilateral symmetry and the main axes of the body are not determined in the chromosomes only, but chiefly in the structure of the protoplasm in the fertilized ovum. All movements in development and growth determining the form of the individual, come to pass according to this structure. On the one hand, disturbances in the bilateral symmetry may depend upon the genes, and on the other hand upon the environment. We know from the experimental embryology that the organism attempts to maintain this symmetrical structure in spite of disturbing influences. This maintenance of a structure originally characteristic of protoplasm, indicates the fundamental rôle of forces in the protoplasm in the development of symmetry, and consequently in disturbances in symmetry, such as transposition of viscera.

The genetics of bronchiectasis and nasal polyps revealed the rôle played by the genes in the constitution. The combination with transposition is apt to demonstrate the rôle of the protoplasm in constitutional differentiation.

However, I will not enter into a closer discussion of the problems of general biology arising in this connection.

SUMMARY

Bronchiectasis and nasal polyps occur in barely 10 per cent of individuals with situs inversus. There is a constitutional interrelation between lesions of the accessory sinuses and the bronchial tract. The combination of bronchiectasis and nasal polyps shows that there is an interrelation between allergy and bronchiectasis, that they may be concurrent phenomena. It is the bronchiectasis, the nasal polyps and the constitutional peculiarity which are hereditary, not the transposition. The frontal sinuses are of usual size in individuals with transposition. The frontal sinuses are probably smaller in individuals suffering from bronchiectasis and nasal polyps. The hereditary mechanism in these conditions is dominant, with a varying probability and mode of manifestation possibly connected with the tendency to transposition. Situs inversus is an expression of the manifold effects of the genes, a complication in development due to different genes, among others the genes causing bronchiectasis and allergy.

ZUSAMMENFASSUNG

Bronchiektasen und Nasenhöhlenpolypen kommen bei nur 10 % von Menschen mit Situs inversus vor. Es liegen konstitutionelle Beziehungen zwischen Affektionen der Nebenhöhlen und des Bronchialbaumes vor. Die Kombination von Bronchiektasen und Nasenpolypen zeigt, dass zwischen Allergie und Bronchiektasen ein Zusammenhang besteht, dass sie miteinander einhergehende Erscheinungen sein können. Die Bronchiektasen, die Nasenpolypen und die konstitutionelle Eigentümlichkeit sind es, die hereditär sind — nicht der Situs inversus. Die Stirnhöhlen sind bei Menschen mit Situs inversus von gewöhnlicher Grösse. Sie sind bei Menschen, die an Bronchiektasen und Nasenpo-

lypen leiden, wahrscheinlich kleiner. Der Erbgang ist bei diesen Zuständen dominant, mit wechselnder Wahrscheinlichkeit und Manifestierungsart, vielleicht verwandt mit der Neigung zu Situs inversus. Der Situs inversus ist Ausdruck der vielartigen Wirkungen der Genen, eine durch verschiedene Genen, u. a. die Bronchiektasen und Allergie erzeugenden Genen, bedingte Entwicklungskomplikation.

RÉSUMÉ

Bronchectasies et polypes nasaux se rencontrent chez tout juste 10 % des sujets à situs inversus. Il y a une corrélation constitutionnelle entre les lésions des sinus paranasaux et celles de l'arbre bronchique. La combinaison d'une bronchectasie avec des polypes du nez montre qu'il y a corrélation entre allergie et bronchectasie et qu'elles peuvent être des phénomènes parallèles. Ce qui est héréditaire, c'est la bronchectasie, les polypes nasaux et les particularités constitutionnelles, mais non le situs inversus. Chez les sujets atteints de cette anomalie les sinus frontaux sont de la dimension habituelle. Ils sont probablement plus petits chez les individus souffrant de bronchectasie et de polypes du nez. Le méchanisme héréditaire, dans ces états, est dominant, avec une probabilité et un mode de manifestation variables, à mettre peut-être en relation avec la tendance au situs inversus. Celui-ci est l'expression des multiples effets des gènes, une complication du développement due aux différents gènes, entre autres ceux qui causent la bronchectasie et l'allergie.

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ÜBER DAS TRAUMATISCH BEDINGTE ANEURYSMA DISSECANS DER AORTA[1]

von

Djin-Yüan Guo

Ein Aneurysma dissecans (An. diss.) entsteht durch Einriss der Intima und der Media eines Gefässes oder der Intima allein, wobei diese Schlitze oft minimal klein sind. Es resultiert augenblicklich ein intramurales Hämatom, welches die Schichten der Gefässwand auseinanderdrängt.

Die Ursachen dieser Affektion sind recht verschiedenartig. Es genügt z. B. bei der Arteriosklerose die Überdehnung der Intima, um einen Einriss hervorzurufen, wenngleich es sich bei dieser Gefässerkrankung meistens nur um einen Durchbruch eines atheromatischen Herdes handelt. Die Ruptur bei luischen Wandveränderungen ist ebenso leicht verständlich. Bei Jugendlichen und Kranken, bei welchen ätiologisch diese Affektionen nicht in Frage kommen, wird das gleiche Krankheitsbild bei abnormer Blutdruckerhöhung beobachtet. So sind mehrere Fälle bei Hypertonikern beschrieben.

KIENBÖCK und WEISS berichten über ein An. diss. bei einer 76 j. Frau, WEISS von 3 weiteren Fällen, alle mit arteriosklerotischer Genese. ESSER sah ein solches intramurales Hämatom bei einer 68 j. Frau, bei welcher die WaR. negativ war. Ein An. diss. mit Verkalkung der Gefässwand fand KRAEN bei einem Luiker, CANIGIANI bei 2 Fällen. OSGOOD und Mitarbeiter konnten zweimal ein Auftreten bei Hypertonie konstatieren. Auch HOLZMANN beobachtete 2 Hypertoniker mit stark, resp. leicht ausgebildeten arteriosklerotischen Veränderungen. REISINGER referiert über 4 nicht traumatische Fälle.

Diesen Beobachtungen liegen primär Erkrankungen des Zirkulationsapparates zu Grunde, erst sekundär bildet sich beim Auftreten geeigneter Bedingungen ein An. diss. aus. Wir müssen diese Krankheits-

[1] Bei der Red. am 10. VIII. 1946 eingegangen.

gruppe deshalb von den durch Unfall entstandenen intramuralen Hämatomen trennen.

Bei diesen traumatisch bedingten An. diss. kann es sich sowohl um direkte Verletzungen handeln als auch um indirekte Läsionen, durch stumpfe Gewalteinwirkung auf den Thorax. In beiden Fällen können Einrisse der Innenwand der Gefässe resultieren, ohne Verletzung der Aussenwand. Durch Einströmen von Blut werden dann die Schichten des Gefässrohres voneinander getrennt. Nach der allgemeinen Ansicht führt ein solcher Einriss in der Intima in kurzer Zeit auch zum Platzen der Aussenwand und zur tödlichen Blutung. In seltenen Fällen bedingt der intramural entstehende Druck einen zweiten Einriss, etwas weiter peripher in der Intima, sodass dem Blutstrom kein wesentlicher Widerstand mehr entgegensteht. Bei diesem Vorkommnis wird die Verblutung vermieden durch das Zustandekommen einer »intramuralen Kanalisation». Diese kann in Form und Ausdehnung durchaus verschieden sein, teils beutel- oder röhrenförmig, teils mit spiraligem Verlauf. HOLZMANN weist eindringlich daraufhin, dass bei zwei Patienten, mit Einrissen an genau gleicher Stelle der Intima, ganz verschiedene Formen des An. diss. resultieren können.

Solche Intimarupturen können vollständig symptomlos verlaufen, wie dies folgende Beobachtungen aus der Literatur schildern:

HEILMANN entdeckte als Zufallsbefund bei der Reihenuntersuchung einen 23 j. Soldaten mit einem An. diss. Dieser Mann hatte alle Strapazen des Militärdienstes ohne irgendwelche Gesundheitsstörung mitgemacht. Ätiologisch liess sich keinerlei Besonderheit erheben, keine traumatische Ursache, keine Überanstrengung, keine Erkrankung, und vor allem kein auffallendes Initialsymptom.

HALL konnte einen kräftigen Sportler untersuchen, der mit 17 Jahren bei einem Wettlauf sich ein solches intramurales Hämatom zugezogen hatte und noch viele Jahre Sport trieb. Vielleicht entstand dieses An. diss. auf Grund einer plötzlichen Überanstrengung mit entsprechender Blutdruckerhöhung während des Wettlaufes. — 15 Jahre später wurde bei der Sektion dieses Mannes ein vollständig ausgeheiltes An. diss. der Aorta gefunden.

Traumatisch bedingte An. diss., welche ausheilen, sind Raritäten. Ein solches wurde z. B. von NISSEN bei einem 36 j. Mann entdeckt, der nach einer Schrapnellschussverletzung diese Affektion, im hinteren oberen Mittelfellraum lokalisiert, davontrug. Das An. diss. war eigross und stand mit einem schmalen Stiel mit der Aorta in Verbindung. Es zeigte sowohl mitgeteilte Pulsation des Aortenbogens als auch systolische Zunahme resp. diastolische Abnahme.

Wir teilen nun noch unseren Fall mit, nicht nur deshalb, weil es sich um eine bemerkenswerte Rarität handelt mit klinisch und röntgenolo-

isch interessanten Aspekten, oder wegen der einmaligen Gelegenheit, öntgenologisch eine ganze Verlaufsserie zeigen zu können, sondern vielehr wegen der praktischen Bedeutung dieser Beobachtungen. Es erheint uns nämlich durchaus möglich, dass man solche Fälle häufiger a Gesicht bekommen kann, wenn man im Anschluss an stumpfe Thoxtraumen darnach sucht. Die Diagnose Commotio cordis, die neuerings im chirurgischen Schrifttum einen breiten Raum einnimmt, drängt azu, auch den Fällen von An. diss. der Aorta vermehrte Beachtung zu henken, da es sich ja um Folgen des gleichen Unfallmechanismus handelt. In diesem Sinne wollen wir unseren Fall aufgefasst wissen:

B. H., 33jähriger Mann, Landwirt.

Familienanamnese: o. B.

Persönliche Anamnese: 1935 Unfall. Der Mann stürzte vom Pferde und fiel mit der Brust auf einen Baumstumpf. Es resultierten Frakturen des Brustbeines und der Rippen. Bei Spitaleintritt beobachtete man kurze Zeit einen auffallend flachen Puls. Die Zirkulationsstörung wurde auf eine damals auftretende doppelseitige Pneumonie zurückgeführt, die in der üblichen Zeit ausheilte.

In den folgenden Jahren war der Mann immer gesund und absolut beschwerdenfrei. Er hatte nie über Herzstörungen zu klagen, auch nicht während der anstrengenden Zeit des Militärdienstes.

1944 wurde bei einer Reihendurchleuchtung das An. diss. entdeckt.

Status praesens:

Mittelgrosser, gesund aussehender Mann von kräftigem Körperbau, in gutem E. Z. — Haut und Schleimhaut: o. B. — Kopf: freibeweglich. — Pupillen: beidseits gleichweit, reagieren gut auf Licht und Konvergenz. — Hals: o. B. — Thorax: kräftiger Bau, symmetrische Atemexkursionen beidseits gleich und ausgiebig. In Brustbeinmitte ist die alte Frakturstelle noch erkennbar. — Lunge: perkutorisch und auskultatorisch o. B. — Abdomen: o. B. — Reflexe: normal. — Herz: normale Grenzen. — Töne: mittellaut, rein, über Aorta und Pulmonalis eher leise. — Puls: 72/min., regelmässig. — WaR.: negativ. — Blutdruck: 130/75. — EKG: o. B. — Blutbild: normal. — Blutsenkung: 5/10 mm. — Urin: o. B.

Röntgenbefund:

Das erste Röntgenbild, vom 19. 6. 1935 (Abb. 1), wurde seinerzeit sofort nach Abheilung der Pneumonie angefertigt. Man sieht auf diesem Bilde eine eigenartige Grössenzunahme und Deformierung des Aortenknopfes und hat dabei den Eindruck, dass sich unterhalb des eigentlichen Aortenknopfes ein zweiter, etwas weniger opaker »Knopf« entwickelt habe. Diese Unterteilung tritt auf dem Kontrollbild nach einem Jahr noch deutlicher hervor. Zwischen dem oberen kleineren, dichten Knopf und dem grossen, breitbasig dem Mediastinum aufsitzenden, etwas helleren, zeigt sich eine leichte Einkerbung.

7½ Jahre später zeigt das Röntgenbild, vom 18. 1. 1944 (Abb. 2), im wesentlichen eine ähnliche Form und Grösse dieses »gedoppelten

Abb. 1.

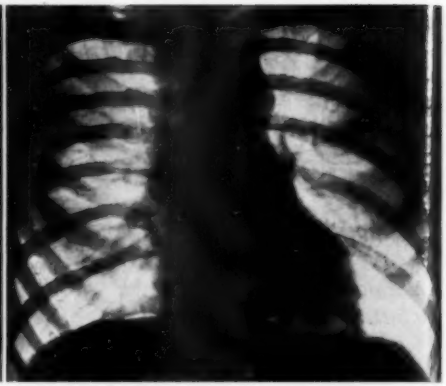

Abb. 2.

Aortenknopfes» wie bei der Kontrolle nach einem Jahr. Wir haben die Oesophagusfüllung herangezogen, um uns besser über die Ausdehnung des Prozesses klar werden zu können. Unterhalb des eigentlichen Aortenknopfes und in Höhe des Manubriumkorpusgelenkes zeigt sich eine fast kreisrunde Schattenscheibe, die lateral das Gefässband des Herzens resp. die deszendierende Aorta überragt, wie aus dem Unterschied der Kontrastdichte ohne weiteres abgelesen werden kann. Die Randzonen zeigen kalkdichte Einlagerungen, wobei der Kalksaum besonders kräftig im linken unteren Quadranten ausgebildet erscheint. Auf dem Originalfilm lässt sich ein millimeterbreiter Begleitschatten ausserhalb des Kalkringes erkennen, der wohl der äusseren Aortenwand entsprechen dürfte. Der eigentliche Aortenknopf zeigt keine Wandinkrustation. Die mediale Begrenzung dieses Gebietes kann dank der Oesophagusfüllung gut beurteilt werden. Die übliche Aortenimpression am Oesophagus ist aboral ganz erheblich verlängert, durchaus entsprechend der Grösse der unteren »Scheibe». Dadurch lässt sich auch erkennen, dass deren Durchmesser etwas grösser ist als der des Aortenbogens. Zwischen dem dichten Scheibenschatten, begrenzt durch den Kalksaum um die Konturen des Oesophagus, zeigt sich wiederum eine schmale Zone, welche etwas heller erscheint. Sie entspricht der Aorten- samt Oesophaguswand.

Bei der Durchleuchtung bewegen sich beide Vorwölbungen, der Aortenknopf und die darunterliegende Scheibe, gleichsinnig. Um dies absolut sicher sagen zu können, haben wir den Patienten noch kymographisch untersucht. Dieser Befund deckt sich durchaus mit dem Eindruck bei der Durchleuchtung. Die Bewegungszacken sind, wie gesagt, gleichsinnig und synchron. Der Bewegungsraum ist lediglich im Gebiete der verkalk-

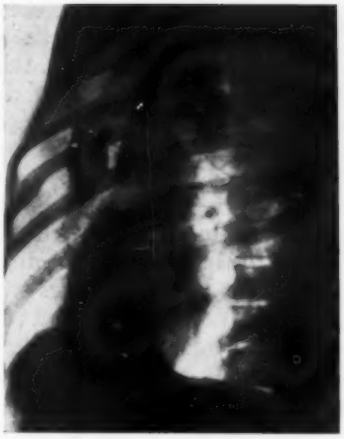

Abb. 3.

ten Zone etwas schmäler, was sich auch an der Form der Zacken ausdrückt. Es handelt sich um mitgeteilte Schwingungen.

Auf der Aufnahme vom 13. 1. 1944 (Abb. 3) im zweiten schrägen Durchmesser ist die Aorta in Höhe ihres Bogens statt in kranialer, in kaudaler Richtung gekrümmt, wodurch eine Doppelhöckerigkeit mit dazwischenliegender Einsattlung entsteht (Form eines Kamelhöckers). In diesem Gebiete ist überdies der Querschnitt der Aorta grösser als normal. In ganzer Länge dieser atypischen Verkrümmung weisen die Wände Kalkeinlagerungen auf. Die aszendierende Aorta zeigt bis zu der spitzwinkligen Umschlagstelle keine sklerotische Zone, anschliessend daran folgt das nach unten durchgekrümmte starre Kalkrohr, welches wirbelsäulenwärts wieder etwas ansteigt, um dann spitzwinklig in die deszendierende, nicht verkalkte Aorta überzugehen.

In Abb. 3 sieht man ausserdem besonders schön die alte verheilte Rippenfraktur und den Bruch des Brustbeinkörpers, der in schlechter Stellung verheilt ist.

Es ist nun interessant ein Bild vom 23. 10. 1936, welches 16 Monate nach dem Unfall ebenfalls im zweiten schrägen Durchmesser aufgenommen wurde (nicht abgebildet) vergleichend zu betrachten. Bereits damals ist eine ähnliche Deformierung nachzuweisen. Zwar besteht noch keine Einsattlung, sondern nur ein auffallend »geradliniger« Verlauf des »Aortenbogens». Irgendwelche Kalkschollen in den Gefässwänden lassen sich noch nicht feststellen.

In der Literatur wird das An. diss. am Aortenbogen röntgenologisch als helles Schattenband beschrieben, das sich schalenförmig dem massiven zentralen Schatten des Aortenknopfes anschmiegt. Dieser Befund lässt sich bei unserem Falle auf den Originalbildern noch weiter differenzieren: Der massive zentrale Schatten des Aortenquerschnittes ist umrandet von einem schmalen Kalksaum, der wahrscheinlich dem verkalkten intramuralen Hämatom entspricht, das sich flächenhaft ausgebreitet hat und nach aussen anschliessend in eine wenig dichte Randzone übergeht, welche als äussere Aortenwand anzusehen ist.

Die Diagnose eines traumatisch bedingten An. diss. der Aorta stellten wir bei diesem 33 j. Patienten, mit fehlenden Zeichen, die für eine Hy-

pertonie, ein Lues oder eine Arteriosklerose sprechen könnten, aus den röntgenologisch sichtbaren Veränderungen im Gebiete des Aortenbogens die im Anschluss an eine schwere traumatische Einwirkung auf den Thorax auftraten und im Lauf der Jahre zu weiteren Ummodellierungen führten. Der Sturz des Mannes vom Pferde mit dem Aufschlagen seines Brustkorbes auf einen Baumstumpf, also ein schweres stumpfes Trauma dürfte den Intimaeinriss ausgelöst haben, der von schweren klinischen Erscheinungen am Zirkulationsapparat gefolgt war. Das rasche Abklingen des bedrohlichen Zustandes kann auf eine »Kanalisation» in der Aortenwand, durch Auftreten eines zweiten Intimaeinrisses in einem peripheren Abschnitt, zurückgeführt werden.

Die Verlaufkontrollen zeigen nun die langsame Umformung des Aortenbogens, mit dem Resultat eines um 180° gedrehten, kraniokonvexen statt -konkaven, Arcus aortae, der durch Kalkinkrustation seine Form bewahrt und sich in ein starres Rohr verwandelt hat. Pathologisch-anatomisch ist die Umwandlung eines intramuralen Hämatoms in eine Kalkkruste durchaus erklärbar. Nach der Verlaufsserie zu urteilen, besteht also ein zeitlicher Zusammenhang zwischen Unfallereignis und Aortendeformierung.

Schwierigkeiten bereitet die Erklärung der eigenartigen Krümmung der Aorta im verletzten Gebiet. Wir müssen uns dabei wieder an die Beobachtungen von HOLZMANN erinnern, der aufmerksam machte, dass bei an gleicher Stelle sitzenden Intimaeinrissen die Form des An. diss. durchaus verschieden sein kann. In unserem Falle dürften die Strömungsverhältnisse im »kanalisierten» intramuralen Hämatom für die »Ab- resp. Durchknickung» des Arcus aortae verantwortlich sein.

Die Prognose eines An. diss. ist ausserordentlich ernst. Mehr als $^3/_4$ aller Patienten sterben innerhalb weniger Minuten, die restlichen innerhalb von einigen Tagen, Wochen, teils auch Monaten. Aus der Literatur sind nur vereinzelte Fälle bekannt, die mehrere Jahre lebten. In diese letzte Kategorie gehört wohl auch unser Patient. Der Mann lebt heute noch, 11 Jahre nach dem Unfall, ohne Beschwerden. Die Affektion wurde zufällig bei einer Reihendurchleuchtung entdeckt. Dies gibt Veranlassung auf solche Fälle aufmerksam zu machen, da diese bis jetzt immer noch als grosse Rarität angesprochen werden, vielleicht aber, bei systematischem Suchen im Anschluss an stumpfe Thoraxtraumen, gar nicht so selten sind. Auch die Commotio cordis wurde ja häufiger beobachtet nachdem von verschiedenen Seiten auf die Möglichkeit ihres Auftretens bei solchen Unglücksfällen aufmerksam gemacht worden war. Vielleicht zeigen sich bei diesem Vorgehen auch Fälle von An. diss., die unter der »Flagge» Commotio cordis »segelten».

Das rasche Abklingen der klinischen Erscheinungen beim An. diss. führte wohl dazu, dass man diese Patienten meistens nicht systematisch

ınd vor allem nicht röntgenologisch weiterkontrollierte. Die Beschwerlenfreiheit illustriert unseren Fall, fast möchte man sagen, klassisch. Sie lauert trotz schwerster Arbeit als Landwirt schon 11 Jahre an. Welcher Leistung der Zirkulationsapparat bei diesem Manne fähig ist, zeigt sich ıber wohl am besten darin, dass er bei der ausserordentlich schweren Sportprüfung einer ganzen Division der Schweizer Armee (»Divisionsmeisterschaft») den 5. Siegerpreis bekam. Er wurde wohl auch deshalb ɔei der klinischen Untersuchung und Abklärung seiner Affektion in einer Militärsanitätsanstalt für 100 % arbeitsfähig erklärt.

ZUSAMMENFASSUNG

Es wird über ein traumatisch bedingtes Aneurysma dissecans am Aortenbogen berichtet, das nicht allein wegen der Rarität, sondern auch wegen der röntgenologischen Verlaufsserie interessiert. Die Erscheinungsformen und ihre Änderungen im Laufe der Jahren konnten eingehend studiert werden. Das rasche Abklingen der klinisch bedrohlichen Initialerscheinungen bei einem An. diss. und die spätere Beschwerdenfreiheit führten wohl dazu, dass diese Fälle — vielleicht irrtümlich — als extreme Seltenheit im Schrifttum angesprochen werden. Bei stumpfen Thoraxtraumen muss man nicht nur an eine Commotio cordis, sondern auch an ein An. diss. denken.

SUMMARY

Report is given of an aneurysma dissecans of traumatic origin at the aortic bend which is not only interesting on account of its rarity but also because of the regular radiologic control of its development. The phenomena connected with its appearance, and their modification in the course of years could be closely studied. The rapid regression of the clinically threatening early symptoms in an aneurysma dissecans and the absence of symptoms afterwards are probably the cause that these cases are considered in the literature as extremely rare. In blunt thoracic traumas one must not only think of a commotio cordis but also of an aneurysma dissecans.

RÉSUMÉ

Relation d'un cas d'anévrysme disséquant, d'origine traumatique, de la crosse de l'aorte, qui n'est pas seulement intéressant par sa rareté mais encore par le contrôle radiologique régulier de son évolution. Les phénomènes liés à son apparition, et leurs modifications au cours des années, purent être étudiés de façon approfondie. La régression rapide des symptômes cliniques menaçants du début, dans un anévrysme disséquant, et l'absence ultérieure de troubles ont probablement conduit à considérer ces cas, dans la littérature, et peut-être à tort, comme des raretés extrêmes. Dans les traumatismes contondants du thorax il ne faut pas seulement penser à une »commotion du coeur», mais aussi à un anévrysme disséquant.

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(HEAD: PROF. ÅKE ÅKERLUND)

ROENTGEN DIAGNOSIS OF PHLEGMONOUS GASTRITIS[1]

by

K. Lindblom

Phlegmonous gastritis is a suppurative lesion of the stomach, chiefly involving the submucosa, most frequently diffusely like an erysipelas but less frequently localized as a carbuncle (LEITH, and others). The total number of cases reported in the literature is about 400. With few exceptions the lesion was diagnosed by necropsy: after some days of severe epigastric pains, usually to the left of the midline, fever, and as a rule vomiting, death took place with symptoms of a septic condition and peritonitis, originating from the upper part of the abdomen. A small number of cases survived and were verified at operation or roentgen examination, or diagnosed by vomiting of pus.

As was pointed out by SUNDBERG and others the clinical signs were as a rule insufficient for the recognition of a gastric phlegmon. Before the era of the modern chemotherapy the practical value of an accurate diagnosis of the lesion was negligible, because no known treatment affected the course of the condition. Nowadays, however, as the possibilities of cure have greatly increased, the diagnostic problems have grown important.

Roentgenological studies of phlegmonous gastritis were made in nine cases, described by OLSSON, ROTHERMEL, WEISS, BEYER, VASS & SIRCA, and CUTLER & HARRISON. Only five of these cases were acute or subacute, and only two of them were diffuse. In spite of the inhomogeneity of the material, the roentgenographical changes seemed to be characterized by a smothened surface of a narrowed lumen with or without remnants of thick mucosal folds. In the prepyloric region the narrowing of the lumen caused retention of the barium. One case reported by OLSSON showed an abscess cavity filled with barium.

The roentgenological findings of obliterated muscosal folds and narrowed lumen correspond thoroughly to the *anatomical* feature of the lesion. The enormous edema and the cellular infiltrations are particularly

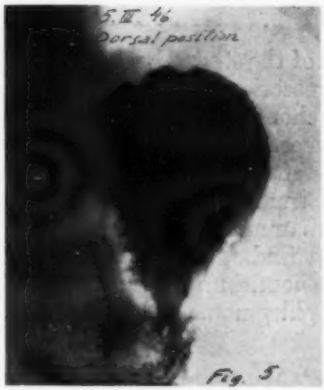
[1] Submitted for publication, July 13, 1946.

Fig. 3

Fig. 4

marked in the submucosa, which may have a thickness of 1—2 cm (FINK, VASS & SIRCA, and others). On account of a submucosal swelling the folds are obliterated, the same in the stomach in cases of phlegmonous gastritis as in the ileum in a terminal ileitis. Necrosis and perforating abscesses lead to defect in the wall (ROSENTHAL & TOBIAS). Histologically the character of the lesion may vary from acute to subchronic without influencing the macroscopical view seen in the roentgenogram.

The pathogenesis of the phlegmon is an infection, mostly by streptococci, from a distant or an adjacent focus, or a local one as a gastric ulcer or carcinoma, or a perforating foreign body (SCHNEITLER). It is



Figs. 1—6. Roentgenograms of a case of postoperative phlegmonous gastritis. Fig. 1 before operation. Fig. 2 during infection climax. Figs. 3—4 (a. p. and lateral views) three days later. Figs. 5—6 recovery. Note the disappearance and recurrence of mucosal folds in the fornix, and the increased and decreased distance to the lung contour.

important to know that a gastric operation may start the process. PERSSON has brought together thirteen cases of postoperative phlegmonous gastritis. A few days after a gastric resection a phlegmon came with fever, local pain, with or without signs of gastric retention, peritonitis, and death. It was noticed that the resection specimens of such cases showed marked infection in the ulcer region.

Case report

The patient, a man aged forty-seven, had recurrent symptoms of a gastric ulcer since 1930. His ulcer was demonstrated by roentgen examination on October 31, 1945, and January 12, 1946. On account of the recurrences and the prominent and suspicious margins of the ulcer a gastric resection was performed on January 29, 1946. The pathologic examination revealed a chronic ulcer with hyperplastic callus formations and exuberant inflammatory changes in the bottom of the ulcer. On the twelfth day the temperature rose, fell during two days of chemotherapy, rose again and grew high and remitting. The patient complained of tenderness in the left epigastrium, local pain and nausea but no vomiting. Muscular spasm, leucocytosis, and increased blood sedimentation occurred, and albumin, hyalin and granular casts appeared in the urine. During this period roentgen examinations (February 18 and 20) revealed a total obliteration of the mucosal folds of the gastric fornix, originally normal, while the mucosal pattern of the corpus was faintly visible by broad foldings. The distance from the gastric lumen to the lower contour of the lung was increased. On February 20 chemotherapy by penicillin and elkosin began. A few days later the temperature was normal, and the epigastric symptoms and the leucocytosis etc. had disappeared. A repeated roentgen examination on March 5 revealed a recurrence of mucosal folds in the fornix.

Comment

The case described had a chronic ulcer of the stomach with histologica signs of inflammation. After a gastric resection clinical features of ar inflammatory condition in the left hypochondrium occurred. Roentger examinations revealed obliteration of mucosal folds, previously normal and signs of thickening of the gastric wall. After healing by chemotherapy the mucosal pattern again returned to normal and the thickness of the wall decreased. No other location of an inflammatory process than in the gastric wall itself might explain roentgen findings of this type, and in cases of a septic condition in the left hypochondrium these findings might be considered pathognomonic of a gastric phlegmon.

SUMMARY

A case of phlegmonous gastritis is reported. The phlegmon was secondary to a resection on a gastric ulcer, and was cured by chemotherapy. By the obliteration of the mucosal folds and the signs of the increased thickness of the gastric wall the lesion could be recognized roentgenologically and differentiated from an inflammatory process of extraventricular location.

ZUSAMMENFASSUNG

Es wird über einen Fall von phlegmonöser Gastritis berichtet. Das Phlegmone trat sekundär zu einer Resektion eines Magengeschwürs auf und wurde mittels Chemotherapie geheilt. Durch die Obliteration der Schleimhautfalten und die Anzeichen vermehrter Dicke der Magenwandung konnte das Leiden röntgenologisch erkannt und von extraventrikulär gelegenen entzündlichen Vorgängen unterschieden werden.

RÉSUMÉ

Relation d'un cas de gastrite phlegmoneuse. Le phlegmon était consécutif à une résection pour ulcère gastrique et fut guéri par chémothérapie. C'est par la disparition des plis de la muqueuse et par les signes d'épaississement de la paroi stomacale que la lésion put être reconnue aux Rayons Roentgen, et distinguée d'un processus inflammatoire extrinsèque.

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A SYSTEM OF FORMULAE AND CURVES BEARING ON THE DISTRIBUTION OF ENERGY IN THE CONTINUOUS ROENTGEN SPECTRUM[1]

by

R. H. de Waard

The spectrum of the radiation emitted by a roentgen tube is partly a line spectrum and partly continuous. The wavelengths of the spectral lines are characteristic of the material of the anode: the continuous spectrum, however, is almost independent of this material, and the distribution of energy in this spectrum is chiefly determined by the high tension acting on the tube.

I. Physical Fundamentals

In this paper will be given a series of formulae and curves giving quantitative information on the distribution of energy in the continuous roentgen-spectrum. The calculations by which these formulae and curves were obtained have been given in another paper[2], and it is shown there that they are in reasonable agreement with the available experimental evidence. The starting point is a simple assumption suggested by KULENKAMPFF[3] as an outcome of the results of a series of important measurements. This assumption is that the distribution of energy is essentially given by a system of parallel straight lines as shown in fig. 1. Here every line represents the distribution of energy corresponding to a definite value of the high tension acting on the tube, and the representation is such that the energy emitted by the tube per second in the range between the frequencies ν_1 and ν_2 is proportional to the area indicated by hatching in fig. 2.

[1] Submitted for publication, July 31, 1946.

[2] R. H. de Waard, Proc. Kon. Ned. Akad. v. Wetensch., Amsterdam, 49, 944—944 and 1011—1015, 1946.

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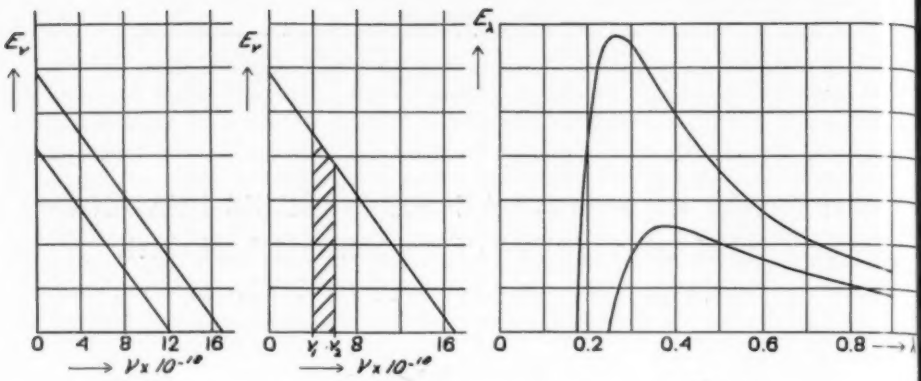

Fig. 1. Fig. 2. Fig. 3.

Fig. 1. Straight lines giving the theoretical relations between $\overline{E}_\nu$ and ν for the constant tensions $V = 70$ kV (upper line) and $V = 50$ kV (lower line).

Fig. 2. Theoretical $\overline{E}_\nu$, ν-line for the constant tension $V = 70$ kV.

Fig. 3. Theoretical $\overline{E}_\lambda$, λ-curves corresponding to the straight lines of fig. 1.

We see from fig. 1 that to every value of the high tension V corresponds a definite maximum frequency ν_0. It follows from DUANE and HUNT's famous quantum relation that

$$\nu_0 = 2.43 \times 10^9 V \quad \ldots\ldots\ldots\ldots \quad (1)$$

if V is expressed in kilovolts.

The straight lines of fig. 1 give the distribution of energy over the various frequencies. To any of them corresponds a definite distribution of energy over the various wavelengths. The latter distributions are graphically represented in fig. 3 and we see that the curves in question are essentially different from the lines in fig. 1. To every maximum-frequency corresponds a minimum wavelength λ_0 which is given by the formula

$$\lambda_0 = \frac{12.3}{V} \quad \ldots\ldots\ldots\ldots \quad (2)$$

in Ångström-units if V is expressed in kilovolts.

Fig. 1 shows that $\overline{E}_\nu$ is proportional to $\nu_0 - \nu$. As, according to experimental evidence, it is also proportional to the tube current i we shall have

$$\overline{E}_\nu = \overline{K} i (\nu_0 - \nu) \quad \ldots\ldots\ldots\ldots \quad (3)$$

where $\overline{K}$ is a factor of proportionality characteristic of the roentgen tube.

From this formula we can derive the new formula

$$\overline{E}_\lambda = \overline{L}i\left(\frac{1}{\lambda_0} - \frac{1}{\lambda}\right)\frac{1}{\lambda^3} \quad \ldots\ldots\ldots\ldots \quad (4)$$

corresponding to the curves of fig. 3 in which figures a new factor of proportionality $\overline{L}$.

For various reasons it cannot be expected that the formulae (2) and (4) represent the actual distribution of energy of the radiation leaving a roentgen tube by its window. In the first place this radiation has traversed the window, and secondly, as we may expect that it originates some distance under the focal area, it has probably passed through a sheet of tungsten as well. Thus, on leaving the tube, the radiation emitted has been subject to the influence of at least two filters.

Now, in many cases, the influence of a filter can be described mathematically by a simple formula. In most substances the coefficient of enfeeblement μ is given by an expression of the form

$$C\lambda^3 + \sigma$$

where C and σ are constants characteristic of the substance in question. If d is the thickness of a filter of this substance a radiation of wavelength λ incident on it at a right angle is enfeebled in the proportion

$$e^{-\mu d} = e^{-d\lambda^3 - \sigma d}.$$

In case of more filters the proportion is

$$e^{-\mu_1 d_1 - \mu_2 d_2 \ldots\ldots} = e^{-(C_1 d_1 + C_2 d_2 + \ldots)\lambda^3 - (\sigma_1 d_1 + \sigma_2 d_1 + \ldots)}$$

and so it has the form

$$e^{-f\lambda^3 - g}$$

where

$$f = C_1 d_1 + C_2 d_2 + \ldots. \text{ and } g = \sigma_1 d_1 + \sigma_2 d_2 + \ldots.$$

There is, therefore, every reason to expect that the radiation emitted by a roentgen tube acting under the influence of constant tension will show a distribution of spectral energy which can be characterized by an equality of the form

$$E_\lambda = \overline{E}_\lambda e^{-f\lambda^3 - g} = \overline{L}i\left(\frac{1}{\lambda_0} - \frac{1}{\lambda}\right)\frac{e^{-f\lambda^3 - g}}{\lambda^3}$$

Now exact measurements have not been carried out with tubes acted upon by constant tensions, and so there is no direct experimental evidence by which the formula obtained can be tested. Experiments carried out with other forms of tension, however, make it probable that the formula provides a good approximation of facts if $-\lambda$ being expressed in Å $-f$ is given a value of about 3 or 6. We will denote this value by f_i and the corresponding value of g by g_i; f_i and g_i are then the characterics of a

filter which we will call the intrinsic tube filter. Of the two quantities f and g_i, however, only f_i is of real importance; g_i and $\overline{L}$ can be accounted for by a single constant

$$L = \overline{L} e^{-g_i}$$

and so the formula for E_λ can be transformed into

$$E_\lambda = Li\left(\frac{1}{\lambda_0} - \frac{1}{\lambda}\right)\frac{e^{-f_i\lambda^3}}{\lambda^2} \quad \ldots\ldots\ldots \quad (5)$$

If external filters are traversed as well we have

$$E_\lambda = Li\left(\frac{1}{\lambda_0} - \frac{1}{\lambda}\right)\frac{e^{-f\lambda^3 - g}}{\lambda^2} \quad \ldots\ldots\ldots \quad (6)$$

where

$$f = f_i + f_1 + f_2 + \ldots. \text{ and } g = g_1 + g_2 + \ldots. \quad \ldots. \quad (7)$$

In order to give an impression of the contribution to f_i which is due to the window of a roentgen tube we will calculate this contribution for the case where this window is a 0.01 cm thick aluminium foil.

If λ is expressed in Å and d in cm we have $C_{Al} = 37$ and so the corresponding value of the contribution Cd — *i. e.* 0.37 — is small in comparison with the total value of f_i of about 3 to 6. Much more important are the thin coats of tungsten which often cover the internal surface of a window. According to a formula given by W. H. and W. L. BRAGG[1] we have $C_{W_0} = 6350$, and so a 0.0001 cm thick coat gives a contribution of no less than 0.635. In a tube in regular use f_i will, therefore, gradually increase.

Formula (6) gives the distribution of spectral energy of the roentgen-radiation in question with a fair degree of accuracy. A reasonable impression of this distribution, however, can also be derived from the minimum wavelength λ_0 and from the wavelength λ_m to which corresponds the maximum value of E_λ. Now the latter wavelength can be determined in a simple way. For this purpose we introduce the angle φ_m given by the formula

$$\cos \varphi_m = \frac{\lambda_0}{\lambda_m} \quad \ldots\ldots\ldots\ldots \quad (8)$$

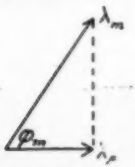

Fig. 4. Physical interpretation of the angle φ_m where $\lambda_p = \lambda_0$ in the case of constant tension.

The physical meaning of this angle is shown in fig. 4; it is a useful measure of the inhomogeneousness of the radiation in question and we will, therefore, call it the angle of inhomogeneousness. It can be shown to satisfy the equation

$$f\lambda_0^3 = \cos^3 \varphi_m \frac{\cos \varphi_m - \frac{2}{3}}{1 - \cos \varphi_m} \quad \ldots\ldots\ldots \quad (9$$

[1] X-rays and crystal structure, London 1924, p. 42.

nd when f and V are known this equation can be easily solved with he help of fig. 5. Indeed, we can first calculate λ_0 from formula (2), next etermine the value of $f\lambda_0^3$, then read from fig. 5 the corresponding value f cos φ_m, and finally derive λ_m from the relation

$$\lambda_m = \frac{\lambda_0}{\cos \varphi_m}.$$

he wavelengths λ_0 and λ_m are useful characteristics of the composition f the roentgen radiation which after being emitted by a tube acting under onstant tension has traversed a definite filter.

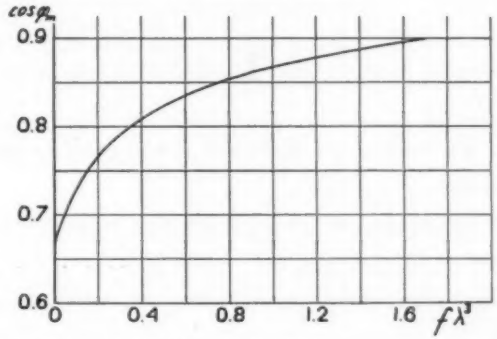

Fig. 5. Curve giving the relation between cos φ_m and $f\lambda_0^3$.

II. Epitome of Formulae and Curves Applying to Different Forms of High Tension

The considerations given in the preceding section apply to cases of constant high tension. They can be extended, however, to several cases where other forms of high tension are concerned, and we will now mention the respective results. These results can be suitably represented in a somewhat different form, and for the sake of uniformity we will give the results applying to cases of constant tension in this form as well.

A. Formulae of general validity.

We denote by V_p the maximum value of the high tension acting on the tube, and by λ_p the minimum wavelength corresponding to this tension, *i. e.*

$$\lambda_p = \frac{12.3}{V_p} \quad \ldots\ldots\ldots\ldots\ldots (10)$$

(n the case of constant tension we have, obviously, $V_p = V$ and $\lambda_p = \lambda_0$.)

Next we introduce the angle φ determined by the formula

$$\cos \varphi = \frac{\lambda_p}{\lambda} \quad \ldots\ldots\ldots\ldots (11)$$

We further put

$$E_\lambda = \frac{Li}{\lambda_0} B_\varphi \frac{e^{-f\lambda^3 - g}}{\lambda^2} \quad \ldots\ldots\ldots\ldots (12)$$

where

$$f = f_0 + f_1 + f_2 + \ldots. \quad \ldots\ldots\ldots\ldots (13)$$

and

$$g = g_1 + g_2 + \ldots.$$

It can be shown that B_φ is then a function of φ which is different for different forms of high tension. The different functions are given in the following survey.

B. Formulae, equations and curves valid in special cases.

1. *Constant tension*

Fig. 6 gives the course of the high tension. B_φ is given by the formula

$$B_\varphi = 1 - \cos \varphi \quad \ldots\ldots\ldots\ldots (14)$$

and the corresponding relation between B_φ and $\cos \varphi$ is graphically represented in fig. 7.

The equation for $\cos \varphi_m$ is

$$f\lambda_p^3 = \cos^3\varphi_m \frac{\cos \varphi_m - \frac{2}{3}}{1 - \cos \varphi_m} \quad \ldots\ldots\ldots\ldots (15)$$

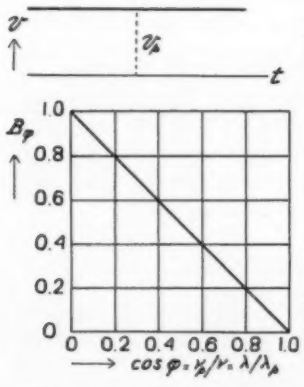

Fig. 6.

Fig. 7.

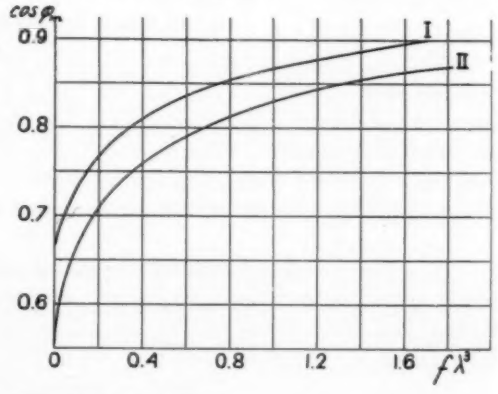

Fig. 8.

Fig. 6. Graphical representation of constant tensions.
Fig. 7. B_φ, cos φ-relation for constant tensions.
Fig. 8. Curves giving the relation between $\cos \varphi_m$ and $f\lambda_p^3$; I for constant high tension, II for high tensions produced by single phase alternating current apparatus.

and it can be solved with the help of curve I of fig. 8 in all cases occurring in practice.

2. *Tension produced by single phase alternating current apparatus.*

Fig. 9 gives the course of the high tension. B_φ is given by the formula

$$B_\varphi = \frac{2}{\pi}(\sin\varphi - \varphi\cos\varphi) \quad \ldots\ldots\ldots (16)$$

and the corresponding relation between B_φ and $\cos\varphi$ is graphically represented in fig. 10.

The equation for $\cos\varphi_m$ is

$$f\lambda_p{}^3 = \cos^3\varphi_m \frac{\varphi_m \cot\varphi_m - \frac{2}{3}}{1 - \varphi_m\cot\varphi_m} \quad \ldots\ldots\ldots (17)$$

and it can be solved with the help of curve II of fig. 8 in all cases occurring in practice.

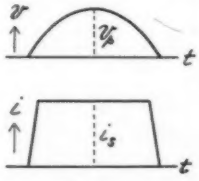

Fig. 9.

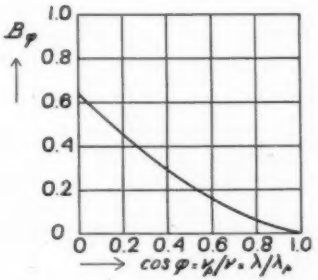

Fig. 10.

Fig. 9. Graphical representation of high tensions produced by single phase alternating current apparatus.

Fig. 10. B_φ, $\cos\varphi$-relation for high tensions produced by single phase alternating current apparatus.

3. *Tension produced by three phase alternating current apparatus.*

Fig. 11 gives the course of the high tension. B_φ is given by different formulae according as $\cos\varphi$ is greater or smaller than $\frac{1}{2}\sqrt{3} = 0.866$. We have

$$B_\varphi = \frac{6}{\pi}(\sin\varphi - \varphi\cos\varphi) \text{ if } \cos\varphi > 0.866 \quad \ldots\ldots (18\,a)$$

and

$$B_\varphi = \frac{3}{\pi} - \cos\varphi \text{ if } \cos\varphi < 0.866 \quad \ldots\ldots (18\,b)$$

and the corresponding relation between B_φ and $\cos\varphi$ is graphically represented in fig. 12.

The equation for $\cos\varphi_m$ is

$$f\lambda_p^3 = \cos^3\varphi_m \frac{\frac{\pi}{3}\cos\varphi_m - \frac{2}{3}}{1 - \frac{\pi}{3}\cos\varphi_m} \text{ if } \cos\varphi < 0.866 \quad \ldots\ldots (19)$$

whilst it is the same as in the preceding case, viz. (17), if $\cos\varphi_m > 0.866$; these equations can be solved with the help of fig. 13 in all cases occurring in practice.

Fig. 11.

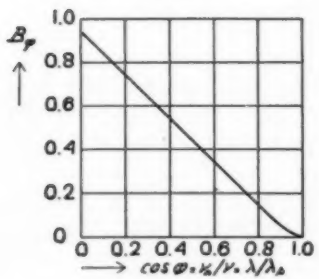

Fig. 12.

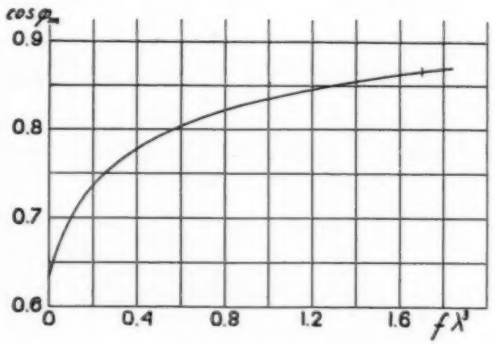

Fig. 13.

Fig. 11. Graphical representation of high tensions produced by three phase alternating current apparatus.

Fig. 12. B_φ, cos φ-relation for high tensions produced by three phase alternating current apparatus.

Fig. 13. Curve giving the relation between cos φ_m and $f\lambda_p^3$ for high tensions produced by three phase alternating current apparatus.

4. *Pulsating tension of Villard's type*

Fig. 14 gives the course of the high tension. B_φ is given by the formula

$$B_\varphi = \frac{1}{2\pi}(\sin\psi - \psi\cos\psi) \quad \ldots\ldots\ldots (20)$$

where the angle ψ is determined by the equality

$$\cos\psi = 2\cos\varphi - 1 \quad \ldots\ldots\ldots (21)$$

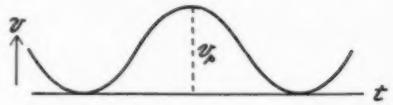

Fig. 14.

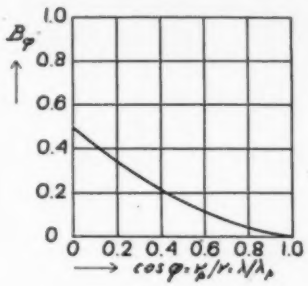

Fig. 15.

Fig. 14. Graphical representation of high tensions produced by apparatus in Villard's arrangement.

Fig. 15. B_φ, cos φ-relation for high tensions produced by apparatus in Villard's arrangement.

and the corresponding relation between B_φ and cos φ is graphically represented in fig. 15.

The equation for cos φ_m is

$$f\lambda_p^3 = \frac{(\cos\ \psi_m + 1)^3\ \{\psi_m(1 + 3\ \cos\ \psi_m) - 2\ \sin\ \psi_m\}}{2\ (\sin\ \psi_m - \psi_m\ \cos\ \psi_m)} \quad . . \quad (22)$$

where

$$\cos\ \psi_m = 2\ \cos\ \varphi_m - 1; \quad . . . . . \quad (23)$$

it can be solved with the help of fig. 16 in all cases occurring in practice.

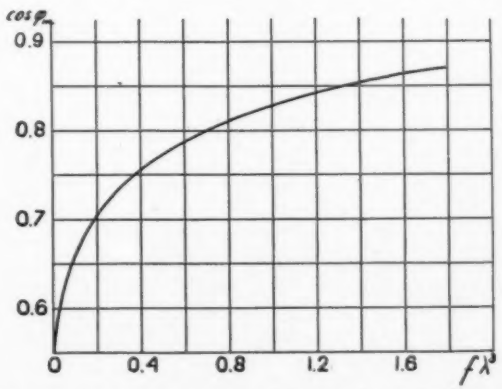

Fig. 16. Curve giving the relation between cos φ_m and $f\lambda_p^3$ for high tensions produced by apparatus in Villard's arrangement.

III. A few Applications

1. A matter of practical importance is the difference in aspect which is said to exist between chest radiographs obtained with apparatus for single phase and for three phase alternating tension. We will therefore determine the composition of the corresponding radiations in case of a peak voltage of 50 kV and of a watersheet of 16 cm thickness being traversed. As to f_i we will assume that $f_i = 4$.

We have

$$\lambda_p = \frac{12.3}{50} = 0.246 \text{ Å}$$

and consequently, as $C_{water} = 2.5$

$$f = f_i + f_w = 4 + 2.5 \times 16 = 44.$$

Hence

$$f\lambda_p^3 = 44 \times 0.246^3 = 0.66.$$

Now fig. 10 shows that in case of single phase alternating tension we have

$$\cos \varphi_m = 0.80 \text{ and } \lambda_m = \frac{0.246}{0.80} = 0.307 \text{ Å},$$

whereas we see from fig. 12 that in case of three phase alternating tension we have

$$\cos \varphi_m = 0.81 \text{ and } \lambda_m = \frac{0.246}{0.81} = 0.304 \text{ Å}.$$

The difference is therefore of very little importance, and when in practice there is a real difference between the radiographs in question this must be due to different peak voltages being applied. If, nevertheless, we wish $\cos \varphi_m$ to be 0.81 in case of single phase alternating tension, we can apply an extra aluminium filter of 0.24 cm thickness. For, as $C_{Al} = 37$, we then have

$$f = f_i + f_{Al} + f_w = 4 + 37 \times 0.24 + 2.5 \times 16 = 53$$

and

$$f\lambda_p^3 = 53 \times 0.246^3 = 0.79,$$

and fig. 10 shows that the corresponding value of $\cos \varphi_m$ is, indeed, 0.81.

It is, however, clear that the application of an extra aluminium filter of 0.24 cm thickness requires a considerable increase of the time of exposure.

2. Another question of practical importance is the difference in composition of therapeutic radiations reaching a patient when apparatus in Greinacher- and Villard-arrangement are used. We will determine this difference for a peak voltage of 180 kV and a filter consisting of 0.15

mm Cu and 1 mm Al whilst f_i is supposed to be $= 4$. We have in this case

$$\lambda_p = \frac{12.3}{180} = 0.0683 \text{ Å}$$

and, as $C_{Cu} = 1310$ and $C_{Al} = 37$

$$f = f_i + f_{Cu} + f_{Al} = 4 + 1310 \times 0.05 + 37 \times 0.1 = 73.2$$

and consequently

$$f\lambda_p^3 = 73.2 \times 0.0683^3 = 0.023.$$

Now, in case of Greinacher-arrangement the tension is approximately constant and curve I of fig. 8 can be made use of.

This figure gives $\cos \varphi_m = 0.685$ and consequently

$$\lambda_m = \frac{0.0683}{0.685} = 0.100 \text{ Å}.$$

In case of Villard-arrangement fig. 16 is applicable, and we have $\cos \varphi_m = 0.595$ and

$$\lambda_m = \frac{0.0683}{0.595} = 0.115 \text{ Å}.$$

The difference is therefore of some importance. If we want to eliminate it by applying an extra copper-filter in the latter case this filter must be more than 0.3 cm thick, and it is clear that this involves a considerable increase of the required times of irradiation.

SUMMARY

In this paper is given a system of formulae from which can be derived the distribution of energy in the continuous spectrum of the radiation which is emitted by a Roentgen tube and has traversed a filter or not; the high tension is supposed to be of one of the following forms: 1. constant tension, 2. tension produced by single phase alternating current apparatus, 3. tension produced by three phase alternating current apparatus, 4. tension of Villard's type. The formulae are based on a simple assumption suggested by experiments published by KULENKAMPFF in 1922 which is in accordance with a theory given by KRAMERS in 1923.

The energy-distribution in question can be largely characterized by the minimum wavelength λ_0 and the wavelength λ_m of maximum intensity. A simple method is given by which these two wavelengths can be determined with the help of some curves. This method is illustrated by two examples of some practical importance.

ZUSAMMENFASSUNG

In dieser Arbeit wird ein System von Formeln vorgelegt, mit denen sich die Energieverteilung des fortlaufenden Spektrums der (gefilterten oder ungefilterten) von einer Röntgenröhre ausgehenden Strahlung berechnen lässt. Es wird angenommen, dass die

Hochspannung von einem der folgenden Typen ist: 1. Konstante Spannung, 2. von einem einphasigen Wechselstromapprat erzeugte Spannung, 3. von einem dreiphasigen Wechselstromapparat erzeugte Spannung, 4. Spannung vom Typus Villard's. Die Formeln fussen auf einer einfachen Annahme, die durch die im Jahre 1922 von KULENKAMPFF veröffentlichten Versuche nahegelegt wird und mit einer von KRAMERS 1923 vorgelegten Theorie stimmt.

Die infragestehende Energieverteilung lässt sich grob durch die Minimiwellenlänge λ_0 und die Wellenlänge λ_m der maximalen Intensität ausdrücken. Es wird eine einfache Methode angegeben, mit der diese zwei Wellenlängen mit Hilfe gewisser Kurven bestimmt werden können. Diese Methode wird durch zwei Beispiele von einer gewissen praktischen Bedeutung veranschaulicht.

RÉSUMÉ

Dans cet article un système de formules est présenté à l'aide desquelles peut être calculée la distribution de l'énergie dans le spectre continu de la radiation émise par un tube Roentgen et ayant traversé un filtre ou non, la haute tension étant d'une des formes suivantes: 1. tension constante, 2. tension due à un générateur à courant alternatif simple, 3. tension due à un générateur à courant alternatif triphase, 4. tension typeVillard. Les formules ont pour base une conception derivée d'une série d'expériences publiées par KULENKAMPFF en 1922, qui est d'accord avec une théorie donnée par KRAMERS en 1923.

La distribution d'énergie en discussion peut être caractérisée en grande partie par la longueur d'onde minima λ_0 et la longueur d'onde λ_m à intensité maxima. Une méthode simple est donnée par laquelle ces deux longueurs d'onde peuvent être déterminées à l'aide de quelques courbes. Cette méthode est illustrée par deux exemples d'une certaine importance pratique.

FROM THE GYNECOLOGICAL DEPARTMENT OF THE RADIUMHEMMET, STOCKHOLM
(CHIEF: PROFESSOR J. HEYMAN)

PRIMARY CARCINOMA OF THE FALLOPIAN TUBE[1]

by

Erik Block

Primary cancer of the fallopian tube is a rare disease. During the years from 1922 to 1945, only sixteen such cases were admitted to the Radiumhemmet, thus less than one case per year.

Since the Radiumhemmet has a larger series of cases than any hitherto reported and since the postoperative radiation therapy has been given according to practically unchanged methods, the publication of this material can be justified even if nothing especially new can be expected regarding the pathology and clinical course of cancer of the tube.

According to obtainable information in the literature, 379 cases have been reported since RENAUD in 1847 first described primary cancer of the fallopian tube. In 1932 NÜRNBERGER in his handbook tabulated the 301 cases which had been published up to that time. In 30 % of those cases, the carcinoma was stated to be bilateral. In most of the cases it was impossible to determine whether it was a primary or a secondary growth. The incidence is greatest in the age group 45—50 but cases have been reported at such an early age as 18 and as late in life as at 73.

Etiology

According to SÄNGER and BARTH cancer of the tube originates in previously inflamed tubes. They state that tubal cancer often is found in a sactosalpinx, that not infrequently it is seen together with tubercular salpingitis (eight cases of coincident cancer and tuberculosis of the tube have been reported in the literature), that inflammatory condition is always present in cases of tubal cancer and that patients with such cancer to a great extent (according to NÜRNBERGER 60 % of the cases) suffer from a primary or secondary sterility. However, they have found only a few followers but many opponents who claim that the inflammatory

[1] Submitted for publication, Sept. 4, 1946.

condition generally is secondary. It is true that in many cases there is no history of a previous pelvic inflammation.

It is of no use to discuss further other theories of its genesis as the etiology of cancer of the tube does not differ from that of cancer in other organs.

Pathology

Generally the cancer starts in the fimbriated end of the tube. According to Mc Goldrick, Strauss and Rao this takes place in 70 % of the cases. There is an early occlusion of the abdominal os with resulting hydro-, hemato- or pyosalpinx. The lumen of the tube gradually gets filled with polypous cancer mass. Only relatively late does the tumour break through the serosa of the tube and invade adjacent organs. A less frequent type of cancer of the tube originates in the isthmus; it spreads more rapidly and is supposed to be more malignant. Early and extensive adhesions to adjacent organs are noticed. The macroscopic findings are from small papillomatous excrescences inside the tube to voluminous tumours of varying consistency and shape.

The microscopic appearance is that of a papillary, a papillo-adenomatous and adenomatous growth. The papillary growth is supposed to be the initial and for tubal cancer typical form while the others are later stages in the development (Liang). However, there may be a primary adenomatous type. Although one type may dominate, cancer of the tube is generally partly papillary, partly papillo-adenomatous and partly adenomatous.

The cancer spreads directly or along the lymphatics. The ovaries are frequently involved, mostly the ovary on the same side but at times also the opposite. Metastases often arise in the uterus either along the lumen of the tube or along the lymph vessels. The former way is the more common.

When the carcinoma extends through the tubal serosa or through the abdominal os, it soon involves the intestines and the pelvic peritoneum. Extension to the bladder has been reported in a few cases only.

Metastases in the lymph nodes are often found in the iliac, aortic and lumbar glands but at times also in the inguinal and supraclavicular glands.

Metastases have been noticed in a number of different organs such as vagina, urethra, kidneys, adrenals, liver, lungs, stomach, diaphragm, spleen and skin.

Symptomatology

Like carcinoma of the ovaries, the tubal cancer long remains latent. Pain is reported to be the most common symptom. It is not of any def-

ilite type. Some authors (v. ROSTHORN, KEITLER, ROBERTS and WEINRUNNER) have described cases with an intermittent type of pain. This is supposed to be due to a varying degree of distention of the sactosalpinx manifesting itself by an intermittent abundant discharge. Although a marked discharge from a hydrosalpinx is rare, it was observed, according to RUGE, in 25 % of the 182 cases of tubal cancer which were reported in 1916.

With reference to the discharge, MARTZLOFF has studied NÜRNBERGER's 301 cases. In 50 per cent of the cases there was no discharge. The other 50 per cent of the cases could be divided into the following four groups, the classification being based upon the character of the discharge.

1. purulent in 20 %
2. sangineous in 40 %
3. profusely serous in 20 %
4. sero-sanguineous in 20 %.

In the presence of a mass in the adnexa, MARTZLOFF considers the sero-sanguineous discharge as pathognomonic of carcinoma of the fallopian tube, provided conditions in the uterus and the vagina being normal.

In cases of tubal cancer, bleeding is not a constant symptom. Irregular periods may depend on other things as most of these patients are in the climacteric. However, many cases of bleeding in the menopause (61 out of NÜRNBERGER's 301) have been described. It has not been explained what causes such hemorrhages in cases of carcinoma of the ovary or the tube. It is hard to imagine that these bleedings are hormonal in nature and caused by a stimulation of the ovaries. Most likely they originate from the tumour itself or from small metastases in the uterine mucosa.

Diagnosis

Because of the infrequency of tubal cancer and its less characteristic symptoms, it is generally impossible to arrive at a correct diagnosis prior to operation. Most cases are diagnosed as tumour of the ovary or chronic salpingitis. Only two authors, DANNREUTER and HOFFMAN, claim that they have made a correct diagnosis preoperatively. An irregular bleeding from an atrophic uterus and the presence of a unilateral tumour in the adnexa made DANNREUTER suspect tubal cancer. MARTZLOFF suggests hystero-salpingography to be of diagnostic value, but as far as is known, tubal cancer has never been diagnosed by such an examination.

Treatment

The treatment is in the first hand surgical, namely removal of the adnexa. Some authors (DIETRICH, NÜRNBERGER *et al.*) have suggested

hysterectomy. However, in so doing they have not considered the desirability of retaining the uterus for postoperative radium application. On the whole, markedly few cases, according to MARTZLOFF (1940) only 22, have been submitted to postoperative radiation. Only one of those has remained well for five years. After a careful review of the literature, MARTZLOFF claims that he does not feel justified in using postoperative radio-therapy.

It should, however, be noticed that of the 22 cases mentioned above only three had been treated with radium. The other 19 were treated by roentgen irradiation only. One case had received both roentgen and radium treatment, the latter because of a coincident cancer of the cervix. Thus combined treatment according to the principles adopted at the Radiumhemmet has not been given to any case. The roentgen intensity administered is not mentioned in most of the cases. Three series of treatment were given in one case, two series in five cases, and one series in the rest.

Some authors (PENCKERT and WAGNER) recommend intra-abdominal roentgen irradiation at laparotomy and believe that they have obtained good results. PENCKERT's patient is free from recurrence after eight and WAGNER's after three years.

Prognosis

The prognosis in tubal cancer is considered to be poor. In the literature only twelve cases are reported which have remained well for a period of five years from the beginning of the treatment. However, a number of cases are reported before the expiry of the five-year period and their further destinies are unknown. Consequently an additional number of cures cannot be excluded. Of the twenty-two irradiated patients related by MARTZLOFF, eight were alive without evidence of the disease at the time of the publication.

The Radiumhemmet Cases of Primary Tubal Cancer

A brief report is given below of sixteen cases treated at the Radiumhemmet. In each individual case an analysis of the diagnosis is made. The microscopic diagnosis has in most cases been verified at the Radiumhemmet Institute of Tumour-Pathology. In connection with this paper, Professor O. REUTERWALL has kindly reviewed the slides. According to his advice, some cases have been excluded because it could not be proved with certainty that they were primary tubal carcinoma.

Case 1. Case No. 396/23. Diagnosis: Bilateral cancer of the fallopian tubes. Age: 52 years. Nulliparous. Menopause since nine months. Past history: »Inflammation» in

t e lower abdomen twice at the age of 30. Present complaint: Abundant, thin, not offens ve discharge for nine months. Pain in the lower abdomen for three months. Frequent i icturitions for one week prior to the admission to the hospital at Sundsvall. Preoper tive diagnosis: salpingitis. Operation: Bilateral salpingectomy on March 15, 1923. Abs ract from the surgical report: The right adnexa difficult to remove because of extensive a hesions and the operation most likely not radical. The diseased left tube was also re- o ved. Microscopic examination revealed bilateral tubal cancer. The slides have not b en traced. Admitted to the Radiumhemmet on April 30, 1923: Uterus retroverted and o normal size. Parametrium normal. Curettage with negative result. Treatment: In the u erus 33 mg Ra-el[1] for 30 hours = 990 mg hrs.[2] Roentgen treatment 2×550 r to one a terior and one posterior field. Seven months later a new roentgen series of 550 r to e ch field. Seven months after the treatment a metastasis, the size of a child's fist in th e abdominal scar and a mass in the pelvis, the size of the fist. Died on March 23, 1925.

Epicrisis: The data are incomplete and the slides not traced. Information regarding the ovaries is lacking but since they were left in situ it is most probable that they were not macrosopically involved. Had the growth originated in one of the ovaries it would have been from the right where the adnexa were reported to form a mass. Considering that ovarian cancer usually metastasizes earlier to the ovary of the other side than to the tubes, this also argues against the supposition of a primary ovarian cancer. Therefore the diagnosis primary tubal cancer is probable but not fully established.

Case 2. Case No. 810/23. Diagnosis: Bilateral cancer of the fallopian tubes. Age: 28 years. Two children. Regular periods until two months before the operation, when a serious hemorrhage occurred and simultaneously pain in the lower abdomen. The pain ceased after a couple of days but a continuous slight bleeding remained. September 13, 1923 (Hospital at Flen): Left salpingo-oophorectomy and right salpingectomy. Abstract from the surgical report: Bilateral tubal cancer. Left ovary surrounded by the tubal tumour. Right ovary normal. Microscopic diagnosis: Adenocarcinoma of the tubes (SUNDBERG). Slides not traced. Admitted to the Radiumhemmet on November 29, 1923: Uterus of normal size, fixed, Slight swelling of parametrium on both sides. Treatment: In the uterus 38 mg Ra-el for 32 hours — 1220 mg hours. Roentgen treatment: Right and left anterior fields 2×500 r to each field; 2×550 r to one posterior field. Examined at the Radiumhemmet the last time in 1935. — Future examinations at Flen. On March 10, 1945 free from evidence of the disease.

Epicrisis: On the whole, the same applies to this case as to Case 1. The record is incomplete and the slides have not been traced. Since both tubes were involved and since the right ovary was reported to be normal, the diagnosis is probably tubal cancer though not definitely established.

Case 3. Case No. 874/24. Diagnosis: Cancer of the right fallopian tube and left ovary. Age: 50 years. Nulliparous. During the last year, slight bleedings of menstrual type every three or four months. Two attacks of abdominal pain seven weeks and one

[1] mg Ra-el = milligram Radium element.

[2] mg hrs = milligram hours. 1 mg hour is the dose given when treating a patient with 1 mg Ra-el for 1 hour.

week prior to admission and one week before admission acute abdominal pain. Admitted to the Ersta Hospital in October 1924. Pelvic examination: Behind and to the right of the normal-sized uterus, a rounded, fixed tumour with a smooth surface, almost the size of a child's head. October 17, 1924 (Ersta Hospital): Bilateral salpingo-oophorectomy. Abstract from the surgical report: Right tube transformed into a sac, the size of a goose egg, filled with a polypous tumour mass. Right ovary not visible. To the left an ovarian cyst, the size of a child's head, also filled with a polypous tumour mass. The left tube apparently normal. Pathological report: Adenomatous tubal cancer of solid and papillary appearance. Admitted to the Radiumhemmet on December 12, 1924: Anteflexed uterus, slightly fixed to the abdominal scar, somewhat enlarged. Parametrium not involved. Treatment: In the uterus 38 mg Ra-el for 30 hours = 1140 mg hours. Roentgen treatment: Right and left anterior field 320 r twice to each field. 340 twice to one posterior field. Died from cancer on March 9, 1925.

Epicrisis: From the case record, it is impossible to obtain a clear conception of this case. The surgeon states that cancer was present in the right tube, that the right ovary is not seen, that the left tube apparently is normal, and that there is a large carcinomatous cyst in the left ovary. The pathologist has evidently interpreted not only the right but also the left tumour as a tubal cancer. In the report which has been given above *in extenso*, nothing is mentioned about the ovaries. The diagnosis of primary tubal cancer is therefore probable although not fully established.

Case 4. Case No. 2029/26. Diagnosis: Bilateral cancer of the fallopian tube. Age: 53 years. One child. Menopause since a year. For the last seven months a yellowish-brown, thick vaginal discharge bloodstained for the last three months. Frequent micturitions for the last month. Admitted to the Sabbatsberg Hospital on February 8, 1926. Above the cervix an irregular tumour, the size of a child's head, broadly adherent to a tumour, the size of the fist, in the Douglas' pouch. Microscopic examination of curettings: No cancer. Preoperative diagnosis: Myoma. February 19, 1926 (Sabbatsberg Hospital): Bilateral salpingo-oophorectomy. Abstract from the surgical report: On the right side an ovarian cyst, the size of the fist, over which ran the thickened tube. When the tube was cut open, its whole mucosa was found to be transformed into a papillomatous mass. From the right ovary was aspirated a thin fluid. On the left side, the tube was as thick as a thumb and surrounding the normal-sized ovary. Cancer-like tissue in the tube on this side. Extensive adhesions. The cancer has probably involved the pelvic peritoneum. Pathology report: The tumour is composed of cavities into which papillary tumour protudes. Undoubtedly a bilateral tubal cancer (BERGSTRAND). Re-examination (REUTERWALL): The only available slide reveals a mainly papillomatous cancer. No ovarian structures are visible but it is likely that part of the wall of the tube is present. Admitted to the Radiumhemmet on April 10, 1926: Uterus fixed to the abdominal scar and of normal size. On the right side a poorly defined swelling. Roentgen treatment on April 13: Right and left anterior fields 3×320 r to each field, 3×350 r to one posterior field. Radium treatment on April 17: In the uterus 50 mg Ra-el for 30 hours = 1500 mg hours. Half a year later a suspicious pelvic recurrence to the left. Repeated roentgen irradiation 320 and 350 r to the same fields. Metastasis in the abdominal scar two months later. Roentgen treatment of the metastasis: 200 r 3 times. Tumour rapidly growing during the next few monts. Ascites. Died on May 31, 1927.

Epicrisis: Cancer in both tubes and in addition an ovarian cyst on one side. According to the surgical report, the cyst contained a thin, serous fluid. It was probably benign but is not mentioned in the pathologist's report. At the reexamination in 1945 at the Radiumhemmet only one side was available. In this no ovarian tissue was seen but it is probable that part of the tubal wall was present. In this particular case the possibility of a primary cancer in the right ovary cannot be fully excluded. Most likely the case should be interpreted, however, as a primary tubal cancer.

Case 5. Case No. 4303/30. Diagnosis: Cancer of the left fallopian tube and left ovary. Age: 50 years. Three children and one abortion. Regular periods, painful for the last half year. Vaginal discharge for a year. May 10, 1930 (Hospital at Västerås): Left salpingo-oophorectomy. Abstract from the surgical report: Cyst, the size of the fist, with clear, serous content. The left ovary is of the size of a goose egg. Macroscopic examination: Left tube thick as a thumb, due to its distention by tumor masses which do not perforate the tube wall but are spreading to the ovary. Microscopic examination (BEHRING): Adenocarcinoma with pronounced transition to cancer simplex with numerous mitoses. Diagnosis: Tubal cancer with metastasis to the ovary. Re-examination (REUTERWALL) 1931: Ditto, with pronounced tendency to solid growth. Admitted to the Radiumhemmet on June 20, 1930: A mandarin-sized swelling to the left of the uterus. Treatment: In the uterus 44 mg Ra-el for 30 hours = 1320 mg hours. In the vagina 73 mg Ra-el for 30 hours = 2190 mg hours. Roentgen treatment: Right and left anterior and posterior field, 2×300 r to each field. The recurrence decreased but started to grow again after half a year. Repeated roentgen treatment, same dose. Condition unchanged during the following years. The patient received repeated roentgen treatment. Teleradium was also given in 1932. Patient did not complain of any symptoms until the end of 1932 when the cancer perforated to the rectum. After a period of improvement, following repeated roentgen therapy, general deterioration set in towards the end of 1933. Died on January 26, 1934.

Epicrisis: In this case the pathologists without hesitation have registered a primary tubal cancer with a secondary involvement of the ovary. They have not suggested that the condition could have been the reverse. Definite proof for the diagnosis of tubal cancer is not given in the case record. Therefore the diagnosis cannot be regarded as completely established, although it is highly probable.

Case 6. Case No. 5105/34. Diagnosis: Cancer of the left fallopian tube. Age: 65. Uniparous. Menopause at the age of 56. Slight intermittent bleeding for the last two or three months. On May 15, 1934 removal of a benign cervical polyp. On May 28 (Professor AHLSTRÖM): Bilateral salpingo-oophorectomy and supravaginal hysterectomy. Abstract from the surgical report: Left hydrosalpinx, the size of a child's head, slightly adherent to the surrounding. Adhesions also on the right side. Ovaries apparently normal. In the hydrosalpinx serous, brownish fluid. A few centimetres from the uterine end is a plaque one centimetre thick, the size of a shilling. Microscopic examination of the plaque: Adenocarcinoma. Right tube — chronic inflammation. Both ovaries normal (HEDRÉN). Re-examination (REUTERWALL): Papillomatous adenocarcinoma. Admitted to the Radiumhemmet on June 13, 1934. Pelvic examination: A tumour, the size of a hen's egg, to the

left of the cervical stump, a swelling interpreted as probably of inflammatory character. Treatment: In the vagina 80 mg Ra-el for 30 hours = 2400 mg hours. Roentgen treatment: Right and left anterior and posterior fields, 3×400 r to the anterior and 3×430 r to the posterior. Two months later the swelling had disappeared. During the following year and at the last examination on December 9, 1943 free from evidence of the disease.

Epicrisis: A definite case of primary tubal cancer, both clinically and pathologically.

Case 7. Case No. 4934/34. Diagnosis: Cancer of the left fallopian tube. Age 47. Uniparous. Regular periods. During the last year abundant, watery discharge. On May 30, 1934 (Hospital at Norrköping): Bilateral salpingo-oophorectomy and total hysterectomy. Extract from the surgical report: Bilateral hydrosalpinx, to the left the size of a fist and remarkably dense. On its inner surface tumour-like tissue. Pathological report (WAHLGREN): On the top of the left hydrosalpinx a normal-sized ovary. The wall of the tube is partly smooth, partly covered with tumour nodules. No noticeable connection between the ovary and the tube. Malignant tumour resembling a granulosacell tumour. Right tube and ovary: no cancer. Professor REUTERWALL and Dr. WAHLGREN have discussed the possibility of the tumour originating from ovarian tissue in the wall of a tubo-ovarian cyst. Further examination was planned but not pursued. Re-examination of available slides in 1945 (REUTERWALL): The tumour is not a granulosacell tumour but a solid and adenomatous cancer, the structure of which well fits the diagnosis of primary tubal cancer. However, the diagnosis can not be definitely established from the slides available. Since Dr. WAHLGREN suggests that his examination is markedly in favour of a tumour originating from the tube, it seems probable, as far as it is possible to judge, that the diagnosis should be tubal cancer. Admitted to the Radiumhemmet on June 20, 1934. Gynecologic examination: In the vaginal scar some small nodules which are a little suspicious. Rectal examination: Behind the scar dense tissue the thickness of the little finger. Roentgen treatment: Right and left anterior fields 2×390 r to each field. Radium application on June 29 — In the vagina 80 mg Ra-el for 30 hours = 2400 mg hours. Smooth recovery. Control examination in Norrköping the last one on May 31, 1945, when the patient was free from evidence of the disease.

Epicrisis: In this particular case, evidently the examining pathologist does not doubt that the tumour originates from the tube. However, since the microscopic appearance mostly resembled that of a granulosacell tumour, the possibility was discussed of the tumour originating from ovarian tissue in a tubo-ovarian cyst. Repeated investigation was unfortunately not carried out. However, since Professor REUTERWALL in re-examining the slides has found solid and adenomatous cancer, the accuracy of Dr. WAHLGREN's observation of a normal-sized ovary without any connection with the tumour seems left beyond doubt. Therefore the diagnosis is most likely primary tubal cancer.

Case 8. Case No. 765/35. Diagnosis: Cancer of the left fallopian tube. Age: 52. Four children. Long intervals between periods for the last two years. After two months of bleeding, the patient came to the General Maternity Hospital on October 15, 1934. Pathological report on curettings: Endometrial hyperplasia. Since the bleedings continued, the patient was referred to the Radiumhemmet. Examination on January 17

1935: A hazelnut-sized nodule in the left uterine corner. No palpable swelling of the adnexa. No indication for radiological treatment. To report for re-examination in a couple of weeks. However, the patient did not return for five months. Examination on June 26, 1935: Solid, slightly nodular mass the size of a hen's egg on the left side. Normal conditions to the right. The patient was referred to the General Maternity Hospital where a bilateral salpingo-oophorectomy was performed on June 29. Extract from the surgical report: On the left side a tumour, the size of a large hen's egg, fixed to the rectum and to the pelvic wall. (No information regarding the left ovary.) Right ovary and uterus apparently normal. Microscopic examination: Adenocarcinoma (HEDRÉN). Re-examination (REUTERWALL): Slightly differentiated adenocarcinoma with large solid areas. Admitted to the Radiumhemmet on July 16, 1935: Pelvic examination: A few small nodules to the left of the uterus. Roentgen treatment: 3×380 r to three anterior fields and 3×420 r to two posterior fields. Radium treatment on August 14: In the uterus 43 mg Ra-el for 27 hours = 1160 mg hours. A year after treatment an orange-sized tumour appeared on the right side. Second operation on September 18, 1936 (General Maternity Hospital): Removal of a thin-walled ovarian cyst containing cancer and opening of an abscess between the fundus uteri and the sigmoid flexure; the abscess wall most likely cancerous. Examination at the Radiumhemmet nine months later: Uterus fixed, the size of the fist. Admitted for brachyradium treatment on July 16, 1937: 82 mg Ra-el 20 hours in vagina = 1640 mg hours. (Attempts to pass the sound failed.) Same roentgen series as previously. The patient's condition gradually getting worse, the tumour spread to the sigmoid. Died on July 23, 1938, three years after her first operation.

Epicrisis: In this case neither the surgeon nor the pathologist was in doubt regarding the diagnosis of primary tubal cancer. No other possibility has been discussed. However, since there is no report on an examination of the left ovary, the possibility of a primary ovarian cancer cannot definitely be excluded. Still, nothing favours such a supposition and therefore a primary tubal cancer remains as the probable but not definitely proved diagnosis.

Case 9. Case No. 3757/41. Diagnosis: Cancer of the left fallopian tube. Age: 46. For the last two years treated for left breast cancer with lymph-node metastases in the axilla. After pre- and postoperative roentgen irradiation free from evidence of the disease. Nulliparous. Regular periods during the last years but with prolonged intervals. Slight discharge for one to two years, Pain in the lower abdomen for three to four months. During a re-examination at the Radiumhemmet of the breast, the patient reported a discharge and was referred to the gynecological department, on November 12, 1941. In the right groin a fairly suspicious gland, the size of a hazelnut. Pelvic examination: To the right behind the uterus an irregular tumour, mandarin-sized, softer than the uterus, somewhat fixed. Diagnosis: Ovarian tumour. No cancer in curettings. Bilateral salpingectomy on Novemver 25, 1941 (The Radiumhemmet). From the surgical report: Hydrosalpinx on both sides, the size of a hen's egg. Uterus of normal size. Ovaries not mentioned. Macroscopic examination of the removed tubes: Thin-walled left tube, filled with clear, reddish-yellow, thin fluid. Scattered soft nodules, in places bean-sized. Right tube contains a yellowish, clear fluid. the wall is smooth. Microscopic examination: Left — Multiple foci of solid polymorphocellular, papillomatous cancer, and non-specific chronic salpingitis. Right — hydrosalpinx. No structural similarities between the cancer of the tube and that of the breast. Treatment: 40 mg Ra-el for 30 hours = 1200 mg hours in the uterus. Roentgen treatment: Right and left anterior field 3×400 r each field 300+300+400 r to two

posterior fields. Recovery. The last examination on March 21, 1945: Uterus very small anteflexed, movable. No recurrence.

Epicrisis: In this case, no note has been made in the surgical report regarding the ovaries which must have been considered normal since they were left. Evidently the surgeon considered the case to be a bilatera hydrosalpinx and the specimen was left unopened until the time of the pathological examination. There is no reason to doubt the diagnosis o primary tubal cancer.

Case 10. Case No. 12222/41. Diagnosis: Cancer of the right fallopian tube and of the uterus. Age: 57. Menopause for the last two years. Slight, daily bleedings for a year. Discharge for the last three years, gradually increasing, at times offensive. During the last two months intermittent, sudden pain in the abdomen. Operation October 8, 1941 (Hospital at Sundsvall): Curettage and removal of a cervical polyp. Microscopic diagnosis: Benign polyp. Small epithelial foci suspected of being cancerous in nature. On October 14, 1941: Bilateral salpingo-oophorectomy. Extract from the surgical report: Small pelvis occupied by cystic tumour which burst and discharged a brown, serous fluid. Everywhere adhesions to the surroundings. Strong suspicion of primary tubal cancer. Pathologist's report: Macroscopic examination of the right adnexa reveals a cystic tumour with plaque-like, small, papillomatous nodules resembling cauliflower on the inner wall. There is a connection, as wide as a sound, between the tube and the cyst. In this, close to the opening of the tube, is an abundance of small-papillomatous nodules. The microscopic examination shows cancer of a solid and partly papillary adenomatous type resembling the epithelial foci which were found in the curettings. The wall of the cyst contains smooth muscle similarly arranged as in the wall of the fallopian tube. There are also occasional, small, adenomatous spots probably of endometriotic character. Cancer of the same type is present also in the part of the tumour which can be identified as the tube. There is no cancer in the remnants of ovarian tissue, which is fibrous. The macroscopic and above all the microscopic findings incidicate that most likely we are dealing with a primary tubal cancer rather than a primary ovarian cancer. However, it is possible that the cancer may have developed from an adenomatous formation in the ovarian hilus and that it has rapidly penetrated into the tube. The left adnexa normal (REUTERWALL). Admitted to the Radiumhemmet on November 1, 1941: An orange-sized swelling in the abdominal scar. Gynecologic examination: Normal conditions. Uterus not palpable. Treatment: In the uterus 46 mg Ra-el for 27 hours = 1240 mg hours. Roentgen treatment: 3×400 r in four fields, and 3×400 r to the middle of the back. Two months later admitted to the hospital in Sundsvall where multiple metastases in the scar and a tumour in the pelvis, the size of a child's head was noticed. Died on February 6, 1942, four months after the operation.

Epicrisis: It will suffice to refer to the epicritic report made by Professor REUTERWALL. The diagnosis of primary tubal cancer may be regarded as probable, even if not fully established.

Case 11. Case No. 11785/42. Diagnosis: Cancer of the left fallopian tube. Age 56. Nulliparous. Menopause at the age of 50. One month prior to the admission, acute onset of severe abdominal pain. Condition on admission February 1942: Tumour in the lower part of the abdomen, extending up to the umbilicus. Operation on February 9 1942 (Hospital at Gävle): Bilateral salpingo-oophorectomy. Extract from the surgical report: Large, left-sided sactosalpinx adherent to the surroundings. On both sides cysti

varies, the size of a hen's egg. The right tube apparently normal. Report by the pathologists H. HANSON and L. SANTESON: Macroscopic examination: Mostly thin tubal wall with occasional porcelain-white plaques on the inner surface. Corresponding to the narrow portion of the sactosalpinx are a couple of pedunculated nodules, the size of walnuts. In the proximity of these, in various places are found smaller similar ones. Microscopic examination: Both in the large and in the small nodules, which are partly papillary, the cancer is alternatingly solid and adenomatous. No cancer in the wall of the narrow part of the tube, nor in the adherent parts of the pedunculated nodules. No cancer in the right tube. A cystoma in both ovaries but no malignancy. Summary: Cancer developed in an ulterated pyosalpinx. Patient admitted to the Radiumhemmet on August 24, 1942. Pelvic examination — Normal-sized uterus, movable. The right parametrium slightly thickened. Treatment: In the uterus 40 mg of Ra-el for 30 hours = 1200 mg hours. Roentgen treatment: Right and left anterior and posterior fields, 3×500 r to the anterior, 2×500 r to the posterior fields. Three months later 500 r in four fields, anterior and posterior. Patient remains free from evidence of the disease. Last re-examination on June 4, 1945.

Epicrisis: Clinically as well as pathologically fully established primary tubal cancer.

Case 12. Case No. 17335/43. Diagnosis: Bilateral cancer of the fallopian tubes. Age: 45. One child. Periods previously regular. After having missed the period for six weeks, she was bleeding for six weeks prior to the admission to the hospital. During the last year a moderate not odorous, watery, sometimes yellowish discharge. Condition on admission: Billiardball-sized uterus. To the right of and behind the uterus is a well defined tumour of the size of a goose egg. On November 22, 1943 (Hospital at Sundsvall) bilateral salpingo-oophorectomy and total hysterectomy. Extract from the surgical report: Bilateral retort-shaped, thin-walled hydrosalpinx sacs both firmly adherent to the surroundings and containing a brown, serous fluid. Both ovaries of normal appearance connected with the tubes by thin adhesions. Macroscopic examination: Small papillomatous nodules on the inner surface of both tubes, and some small, loose tumour-pieces in the left tube. The ovaries apparently normal. Microscopic examination: Primary, solid cancer, hydrosalpinx and chronic, non-specific salpingitis in both tubes. Nothing noteworthy in the ovaries. No cancer in the uterus (REUTERWALL). Admitted to the Radiumhemmet on February 8, 1943. Pelvic examination: Smooth induration on the left side; slight swelling on the right of the parametrium. Treatment: In the vagina 150 mg of Ra-el for 12 hours = 1800 mg hours. Roentgen treatment: 3×400 r, anterior and posterior, in four fields. Three months later 2×400 r and half a year later 1×400 r in the same fields. At the time of the last examination on May 11, 1945: Free from evidence of the disease.

Epicrisis: Clinically as well as pathologically fully established primary tubal cancer.

Case 13. Case No. 9240/44. Diagnosis: Cancer of the right fallopian tube. Age 56. Two children. Menopause at the age of 52. For the past five or six years, intermittent pain in the right lower abdomen. Fever for two months prior to the operation. Frequent micturition for a couple of weeks. On Febraury 22, 1944 (Hospital at Örnsköldsvik): Right salpingo-oophorectomy. From the surgical report: On the right side a pyosalpinx and a cyst the size of a goose egg. (Nothing reported regarding the left adnexa.) Macroscopic examination: Tube and ovary impossible to separate definitely. Part of the removed specimen consists of a solid wall surrounding a cavity which probably is the lumen of the tube. The rest consists of a thin-walled cyst. Microscopic examination: The cavity of the solid part corresponds with the lumen of the tube. There are areas rich in cells of carcinom-

atous type with differentiation to squamous epithelium in various places. No adenomatous tissue. In the mucous membrane, chronic inflammation with occasional epitheloic tubercles. No cancer in the cystic part. Summary: Simple, multi-locular cyst, chronic purulent salpingitis with patches of tuberculosis, and cancer, probably tubal cancer (REUTERWALL). Admitted to the Radiumhemmet on May 11, 1944. Pelvic examination — The uterus fixed. On the left side a plum-sized mass. Treatment: In the uterus 50 mg Ra-el. Treatment interrupted after five hours because of fever. The temperature remained high. Rapid deterioration. Roentgen examination revealed a tuberculous spondylitis and pulmonary tuberculosis. Death on June 10, 1944. Autopsy disclosed cancerous metastases in the liver and in the aortic glands, as well as an extensive thrombosis of the aorta. No local cancer.

Epicrisis: In this case a primary ovarian carcinoma cannot be definitely excluded. However, Professor REUTERWALL is of the opinion that the case should be mentioned, provided such cases are accepted where the diagnosis has been made with a fair probability. Thus the diagnosis is that of primary tubal cancer, though not fully established.

Case 14. Case No. 13454/44. Diagnosis: Cancer of the left fallopian tube. Age: 57. History of ectopic pregnancy and abortion. Menopause at the age of 51. Discharge during the last five years, bloodstained for half a year. Three months prior to the operation a suspicious tumour of the left ovary was noticed. On June 30, 1944 (General Maternity Hospital): Bilateral salpingo-oophorectomy and total hysterectomy. From the surgical report: Large, left-sided sactosalpinx in direct connection with an enlarged, dense ovary. The right ovary and the uterus are senile. The entire tube is filled by massive tumour. Macroscopic diagnosis: Thin-walled, sac-shaped formation, the size of a fist, narrowing at one end. Mandarin-sized tumour inside the sac. Microscopic examination: In the ovary endometriotic cysts and highly differentiated cancer (A. BERGSTRAND). Re-examination (SANTESON): Uterus and right adnexa without any macroscopic changes. Pieces are taken from the narrow part of the sac-shaped formation, from the thin part of its wall, from the mandarin-sized, solid tumour, from the uterus and from the right ovary. Microscopic — In the uterus foci of internal endometriosis. No cancer. Nothing remarkable in the right ovary. The sac-shaped formation corresponds to the expanded tube. Thus the tumour is situated inside the hydrosalpinx and therefore definitely tubal cancer. To all appearances the carcinoma is of the nature of a cancerous endometriosis. Admitted to the Radiumhemmet on July 17, 1944. Pelvic examination: A swelling, thick as a finger, to the left. Treatment: In the vagina 150 mg Ra-el for 20 hours = 3000 mg hours. Roentgen treatment: 4×400 r, anterior and posterior, in four fields. Three months later 2×400 r in the same fields. After that free from any evidence of recurrence. Last re-examination on February 10, 1945: Free from evidence of the disease.

Epicrisis: This is a case where a hydrosalpinx was originally interpreted as a cystic ovary. The diagnosis was ovarian cancer. This was later changed to tubal cancer. However, regarding the left ovary no information has been given in Dr. SANTESON's report. Since the possibility has not been mentioned, it is apparent that there has been no reason to suspect that the cancer has originated from the ovary. Thus the case can be considered as a probable, although not fully proved, primary tubal cancer.

Case 15. Case No. 15697/44. Diagnosis: Cancer of the left fallopian tube. Age: 0. Nulliparous. Menopause at the age of 51. On June 9, 1941, patient consulted a physician for a vaginal discharge of two years' duration. Lately offensive and sanguineous. Back ache for quite a long time. Treated for colpitis. On November 16, 1942, a tumour was found. On December 7, 1942 (Hospital at Malmö): Left salpingo-oophorectomy. From the surgical report: A tumour the size of the fist in the right adnexa and adherent to the colon and the pelvis. While being freed, it discharged a dirty, brown content. The tumour was thought to originate from the ovary. Both the tubes were sites of old inflammatory changes. The right adnexa were left intact. (No information regarding the appearance of the right ovary.) Pathological examination (SJÖVALL): In the lateral part of the tube towards the fimbriated end, a gradually more abundant proliferation of undifferentiated cancer in the mucous membrane. Infiltration of the muscle layer only in occasional spots. Primary tubal cancer on the basis of a chronic salpingitis. A thin-walled cyst in place of the ovary. Re-examination (REUTERWALL): Mostly solid cancer with certain areas of adenomatous tissue and to a lesser extent also papillomatous structures. Post-operative treatment: Two intrauterine and vaginal applications of radium as well as Roentgen irradiation of two anterior and two posterior fields 3×320 r to each field. Readmitted on November 2, 1942 because of a recurrence in the left wall of the pelvis, in the inguinal glands on the left side and in the abdominal scar. Biopsy. Microscopic diagnosis: Recurrence of cancer. Repeated roentgen treatment: same series as before. Slight decrease of recurrence. On April 5, 1944 electrocoagulation of a new recurrence in the scar. On June 3, 1944, a large recurrence on the left side. In the vagina a tumour the size of a hen's egg. On September 4 biopsy: Cancer with tendency towards papillary formations. On September 20 admitted to the Radiumhemmet: Large recurrence, metastases in both groins and in the abdominal scar and involvement of the bladder. At the request of the patient, treatment was given although it was practically hopeless. Teleradium to the glands and roentgen irradiation 400+500+500 r, anterior and posterior, in four fields. Subjective improvement for a while. Died on February 2, 1945.

Epicrisis: This case may be considered a definite primary tubal cancer. Some uncertainty prevails only with regard to the right adnexa. As they were left there could hardly have been an ovarian cancer on that side.

Case 16. Case No. 360/45. Diagnosis: Cancer of the left fallopian tube. Age: 45. Nulliparous. Married for 21 years. Involuntary sterility. Regular periods. In February 1945 operated upon for cancer of the left breast and postoperative roentgen treatment. No recurrence. Present complaint: Increasing size of the abdomen for the last half year. Condition on May 1, 1945: Rounded smooth tumour in the lower part of the abdomen extending to a level of two fingers below the umbilicus, filling the small pelvis. On May 2, 1945 (Hospital at Gävle): Bilateral salpingo-oophorectomy and supravaginal hysterectomy. From the surgical report: Myomatous uterus, the size of two fists. Ovarian cysts, to the left the size of two fists, to the right the size of a hen's egg. Both tubes the thickness of a finger, stiff, the right one adherent to the abdominal wall. Macroscopic examination: Left tube — Lumen in the uterine part the width of a sound, otherwise homogeneously yellowish-white without visible lumen. Left ovary: Cyst with papillary wall. Right tube: thick-walls and wide lumen. Right ovary: Large cyst with papillary wall. Microscopic examination: Left tube — In the uterine part tuberculosis and findings resembling salpingitis isthmica nodosa. In other sections adenocarcinoma with infiltration of the tube wall. No perforation of the serosa. Left ovary — Papillary cystoma, no indications of transition to infiltratively growing cancer. Right tube — Tuberculous salpingitis. Right ovary — Small cysts. No cancer. Uterus — Endometritis and a small tubercular focus.

A comparison between the specimen of the breast and that of the tubal cancer show that from a morphological point of view they are not sufficiently different to allow th conclusion that we are dealing with two different carcinomas. However, the two carcinomas are definitely primary in loco (REUTERWALL). Admitted to the Radiumhemme on May 13, 1945. Pelvic examination: No pelvic recurrence. Roentgen treatment: 3×40 r, anterior and posterior, in four fields. After this radium — in the vagina 150 mg of Ra-e for $7^1/_2$ hours = 1125 mg hours.

Epicrisis: Clinically as well as pathologically fully established primary tubal cancer.

Summary of the Epicrises

Of the sixteen cases of tubal cancer, six are definitely primary tubal cancer while the remaining ten probably are so. The reason for the uncertainty of the diagnosis in these later cases is in general the lack of complete data, mainly incomplete surgical records. In some cases the specimens have not been available for re-examination, in others the specimens on hand have been incomplete.

Because of the infrequency of primary tubal cancer when compared with primary cancer of the ovaries, it may be assumed that when the first mentioned diagnosis has been made by the clinician or the pathologist it has been well motivated as a rule. The number of diagnosed cases of primary tubal cancer is probably less than the actual number of cases. Since the histological picture does not indicate the origin and therefore the differential diagnosis between primary tubal cancer and carcinoma of the ovary is impossible in advanced cases, most likely some of the cases labelled as tubal cancer will be re-classified as carcinoma of the ovary.

DISCUSSION

Sixteen reported cases of tubal cancer is too small a number for a statistical study. A survey of the results of the radium and roentgen treatment may be of interest.

First a few words regarding the characteristics of tubal cancer, which were mentioned in the beginning.

Of the sixteen cases, four, or 25 per cent, are bilateral. Of the other twelve, nine are left and three right sided. The distribution of the ages are as follows:

28	years	1	case
41—45	»	2	cases
46—50	»	5	»
51—55	»	3	»
56—60	»	4	»
61—65	»	1	case

According to the records, eight cases were in the menopause, four were in the transition period and the other four had regular menstruations.

Etiology

Of the sixteen patients, ten have had children, varying in numbers from one to four. One has had an ectopic pregnancy and an abortion. The others have not been pregnant, and one of these has not been married. Four have thus lived in a sterile marriage. In one case only (No. 1), the history most likely reveals a previous salpingitis. The others have a blank gynecological history. Thus here are no proofs for the statement that an inflammatory condition precedes tubal cancer. However, microscopic examination reveals inflammation in the non-cancerous portion of the tube in five of the twelve cases. In two cases tuberculosis is found coincident with the cancer. In this series there are cases with a preceding inflammatory condition as well as cases in which no such conditions have been noticed.

Pathology

In nine cases the carcinoma is situated in a hydro-, sacto-, or pyosalpinx. In five instances the tumours vary in size from that of a hen's egg to that of the head of a child. In the other two specimens the tubes are fairly evenly thickened. In the hydrosalpinges the cancer is of papillary appearance with foci of varying size while in a few there have been more massive tumours.

At the time of operation the cancer was apparently confined to the tubes in seven of the patients. However, all were more or less adherent to the adjacent organs. In five cases the ovary is involved. Four have extensions to the pelvic peritoneum, and one of them to the uterus as well. Metastases along the lymphatics are not found in any case, neither before nor at the laparotomy. Neither are mentioned metastases to organs outside the pelvis. It should, however, be noticed that in case No. 13, at autopsy three months and a half after the operation, widely spread metastases are found in the liver and the aortic lymph glands.

As mentioned earlier, in four of the sixteen cases both tubes are involved. However, in two of these the slides have not been traced and it must therefore be left undecided whether the cancer was primarily or secondarily bilateral.

Cancer in two different locations is seen in two cases. Comparison of the microscopic appearance proves that the carcinoma is primary *in loco* in both instances. As coincident findings are reported in six cases ovarian cysts and in one instance a fibroid.

Of the sixteen cases of cancer eleven are adeno-carcinomas. Of these eleven, seven are more or less solid, the five papillary.

Papillary growths without adenomatous structure are seen in three cases, two of these of distinctly solid structure.

One of the cases of adeno-carcinoma is most likely of the nature of a cancerous endometriosis. Strangely enough, in one case was found a differentiation into stratified epithelium (case No. 13).

Symptomatology and Diagnosis

Discharge, bleeding and pain are evenly distributed.

Discharge is reported in nine cases. Of these in three it was thin and watery, in two serosanguineous and in one thick. In the other cases a definite description is lacking.

Eight patients complained of metrorrhagia which was marked in two of them. In some instances there has been only a slight serosanguineous flow. Of those patients who had hemorrhages, five were in the menopause.

The pains vary from a deep, constant ache in the back to acute, violent pain in the abdomen. Rise of temperature is noticed only once.

One patient (No. 16) complained of no other symptoms than an increasing size of the abdomen.

The diagnosis was not recognised prior to operation in any of the cases, in four not until the specimens came to the pathologist. The diagnosis was, prior to operation, in most of the cases ovarian tumour, in a few chronic salpingitis, and in one myoma.

Treatment and Prognosis

In the discussion of the results of the treatment, Case 16 is excluded because the treatment is not yet completed. In discussing the radiological treatment, Case 15 is excluded because treated outside the Radiumhemmet.

As could be expected, the essential factor as far as the prognosis is concerned is the spread of the growth. All cases where the cancer was confined to the tubes are alive and free from evidence of the disease, while, the others died within three months to four years after operation.

In those alive, as a rule the operation was more radical than in those who succumbed. In four of the latter cases, the growth involved the peritoneum previous to the operation, the operation thus not being radical.

In four cases where the uterus and the adnexa were removed the patients are alive and free from evidence of the disease, two of these for ten years. This might seem to support the opinion of those who clai n

hat the uterus should be removed simultaneously with the adnexa in ases of tubal cancer. However, there is no indication that such a proce- ure has had a favourable influence on the result in the four cases men- oned.

It is a routine procedure at the Radiumhemmet not to remove the terus in cases of carcinoma of the ovaries. Radium placed in the uterus omes in closer contact with the area of recurrences than that which is laced in the vagina. In tubal cancer there is no reason to deviate from t is principle.

At the Radiumhemmet the radiological treatment of tubal cancer h s followed practically the same principles as in cancer of the ovary namely one intra-uterine or vaginal radium application followed by roentgen treatment to two anterior and two posterior fields. The radium dose has varied, in the uterus 990—1500 mg hours, in the vagina 1800 —3000 mg hours. The roentgen dose has varied. In later years, however, 3×400 r to each of four fields are administered in the first series, followed three months later by a second series of 2×400 r to each field.

None of the cases of tubal cancer has received pre-operative treatment.

As was mentioned above, only twelve of the 479 cases reported in the literature have been cured for five years. Of these only one has received radiation therapy. Of the fourteen cases treated at the Radiumhemmet seven are living and free from evidence of disease for 22, 10, 10, 4, 3, 2 and 1 years respectively. Nothing certain can be said about the prognosis in the last four cases but as they are free from recurrence and as recurrences in those patients who have died have come early, it is possible that one or more of these patients will remain cured for five years.[1]

Although the series is too small for statistical study, it is evident that the results obtained at the Radiumhemmet are more favourable than those obtained earlier.

The effect of radiotherapy can also be studied in the seven patients who have had recurrences. At the time of the operation, in four of these most likely the tumour had involved the pelvic peritoneum and the operation must be considered as incomplete. In three of these recurrences were noticed at the time of the admission to the Radiumhemmet. Two of the remaining three cases, where only the ovaries and tubes have been reported as involved at the time of operation, had a palpable tumour on admission. One of these (Case 13) was in such poor general condition that the treatment could not be completed. Thus in five of the seven cases the prognosis was not particularly favourable. Nevertheless, two of them were kept relatively free from signs and symptoms for four and three years respectively.

[1] The author hopes to be able to give supplementary information regarding these cases after their five-year period has elapsed.

Thus there is little doubt but that radiological treatment according to the principles applied at the Radiumhemmet is of importance for the final result.

Conclusions

The cases reviewed are too few for drawing definite conclusions. However, contrary to the cases reported in the literature, the Radiumhemmet series seems to indicate that tubal cancer is not a hopeless disease provided that a radical operation is performed early and that radiation therapy is administered according to above mentioned method. There is reason to believe that under above mentioned conditions, the result is better in cases of tubal cancer than in cases of cancer of the ovary because the latter generally involves the surrounding organs at an earlier stage.

An improvement of the results might be obtained:

1. by an early diagnosis,
2. by a radical removal of involved tissues, and
3. by a combined intra-uterine radium application and roentgen treatment.

Ad 1. Because of the diagnostic difficulties and the few characteristic symptoms of tubal cancer, a definite pre-operative diagnosis is only exceptionally possible. At times the correct diagnosis can be arrived at by remembering the triad of intermittent pain, sero-sanguineous discharge and adnexal tumour. Whether salpingography is of any value remains to be seen.

In cases of a supposed chronic salpingitis, it may be of importance to remember the alternative of cancer of the tube.

Ad 2. Surgical interference should include the removal of the adnexa on both sides as is the rule in cancer of the ovary. Tubes which are removed on the pre-operative diagnosis of chronic salpingitis, hydrosalpinx, etc., should be opened at once because if cancer should be present, both ovaries must be removed. Unless it is unfit for radium application (myoma, etc.), the uterus should be left *in situ*.

Ad 3. The radiologic treatment should include both postoperative roentgen therapy and intra-cavitary radium application.

The method used at the Radiumhemmet is as follows:

Post-operative treatment:

a. One intra-uterine application of radium, 1500 mg hours or (if the uterus has been removed) 2400 mg hours in the vagina.

b. Roentgen treatment:

1) 3×400 r to each of two anterior and two posterior fields.
2) Same series three months after, 2×400 r and
3) Eventually, after another six months, 1×400 r one treatment a day.

Pre-operative roentgen treatment should be administered whenever there is reason to believe that cancer is present.

SUMMARY

Discussion of the characteristics of carcinoma of the fallopian tube, and report on sixteen cases which have been admitted to the Radiumhemmet, Stockholm.

Although the cases reported are too few for drawing definite conclusions, they seem to indicate that the prognosis of tubal cancer is better than generally reported in the literature, provided that radical operation is done early and that post-operative radiation therapy is administered according to the principles followed at the Radiumhemmet. The possibility of an early diagnosis, the requirement for radical surgery and the guiding principles of the Radiumhemmet method of treatment are mentioned.

ZUSAMMENFASSUNG

Besprechung der Charakteristika des Krebses der Tuba Fallopiae sowie Bericht über 16 ins Radiumhemmet, Stockholm, aufgenommene Fälle.

Obwohl die wiedergegebenen Fälle allzu gering an Zahl sind, um endgültige Schlussfolgerungen zu erlauben, scheinen sie immerhin darauf hinzuweisen, dass die Prognose des Tubenkrebses besser ist, als was im allgemeinen in Schrifttum angegeben wird, vorausgesetzt, dass eine frühe Radikaloperation vorgenommen und nach den im Radiumkrankenhause gebräuchlichen Prinzipien postoperative Strahlenbehandlung gegeben wird. Die Möglichkeiten einer Frühdiagnose, die Notwendigkeit eines radikalen chirurgischen Eingriffes und die führenden Grundsätze der Behandlungsmethode des Radiumhemmet werden erwähnt.

RÉSUMÉ

Discussion des caractéristiques du cancer de la trompe de Fallope, et relation de 16 cas qui furent hospitalisés au Radiumhemmet, Stockholm.

Bien que les cas rapportés soient en trop petit nombre pour permettre d'en tirer des conclusions définies, ils semblent indiquer que le pronostic du cancer de la trompe est meilleur que ne l'impliquent généralement les données de la littérature, à condition qu'une opération radicale soit faite précocement et qu'on mette en oeuvre la radiothérapie postopératoire selon les principes en vigueur au Radiumhemmet. La possibilité d'un diagnostic précoce, les conditions requises pour une intervention chirurgicale radicale, et enfin les principes directeurs de la méthode thérapeutique du Radiumhemmet font l'objet d'une mention.

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FROM THE ROENTGEN DIAGNOSTIC DEPARTMENT OF KAROLINSKA SJUKHUSET, STOCKHOLM
(HEAD: PROF. ÅKE ÅKERLUND)

COMPLICATIONS OF MYELOGRAPHY BY ABRODIL[1]

by

K. Lindblom

The myelography by abrodil means a valuable improvement in the visualization of the details of the lumbar portion of the subarachnoidal space. The original description was made in 1931 by ARNELL and LIDSTRÖM, and the method has been used in more than 700 cases, most of them during the last year. During that year complications were reported, and it was necessary to make a critical examination of the cases from a technical standpoint. Through the kindness of the Swedish roentgenologists I am able to describe the experiences in 721 cases of abrodil myelography, brought together and discussed at the meeting of the Swedish Society of Radiology in November 1945.

The myelographies by abrodil have been performed by two different techniques. The original method described by ARNELL implies an examination in prone, supine, oblique, and lateral positions and vertical direction of rays. In the modified form by LINDBLOM the procedure is performed in a lateral position and horizontal rays. In the latter position with the head end somewhat raised a sufficient lumbar anesthesia is obtained by 1—2 cc of 5 percent novocain. As a prophylaxis against a fall in blood pressure ephedrin is used. Immediately after the examination the patient lies in a horizontal position for one day, which is a sufficient time if the puncture needle is very thin. The contrast medium is 10 cc of 20 percent abrodil or skiodan. KLASON recommends the use of 20 percent intron but it has been used only in a small number of cases.

Complications were reported in more than 54 cases. As the myelography by abrodil must be preceded by a lumbar puncture and anesthesia the complications might be caused by the lumbar puncture itself, or the anesthesia, or the contrast medium.

[1] Submitted for publication, July 13, 1946.

The complications are grouped as follows:

1. Headache for some days — 3 + many cases.
2. Headache and stiff-neck for some days — 2 cases.
3. Headache, stiff-neck, and for two days a paresis of the bladder — 1 case.
4. Shock within 5—30 minutes — 22 cases.
5. Shock 1—3 hours after the myelography — 8 cases.
6. Shock 3—24 hours after the myelography — 2 cases.
7. Lumbar pains during the injection of the contrast medium — 4 cases.
8. Lumbar pains soon after the injection of the contrast medium — 5 cases.
9. Hyperesthesia and latent spasms 3 hours after the myelography — 2 cases.
10. Manifest spasms in the legs after the myelography — 2 cases.
11. Secondary shock, and paralysis of the legs and the sphincters for weeks — 3 cases.

The complications in the groups 1—3 may be the consequences of the lumbar puncture itself. As a rule the lumbar needle had the usual thickness with a diameter of 1 mm or more, a corresponding hole, and an abundant leakage of spinal fluid. In many cases the head end was raised for hours after the examination, which facilitated the leakage.

The complications in the groups 4—6 include the cases of shock. In spite of the fact that most cases were prepared by ephedrin etc. a sharp drop of blood pressure might happen soon after the injection of the contrast medium. The shock is assumed to be secondary to an irritation by the opaque solution on account of an incomplete anesthesia. The raised head end of the table facilitates the entrance of a shock especially when this position remains for hours. In one case the patient was examined in an upright position and the shock appeared within a few minutes. No definite influence of the kind of anesthetic drug could be traced.

The complications in the groups 7—8 including the pains after the injection of the opaque solution must be attributed to the contrast medium itself. Pains appeared after the use of 20 percent abrodil as well as intron. The anesthetic medium was novocain, pantocain, or heavy decicain. Sharp pains appeared in those cases only in which the heavy decicain was used. The high specific gravity of this solution causes a too definite sedimentation in the spinal fluid. The effect is that the anesthesia will not reach as high as the opaque solution.

The hyperesthesia and latent spasms in group 9 were noticed in two cases 3 hours after the myelography. A dose of 0.08 gm novocain and 0

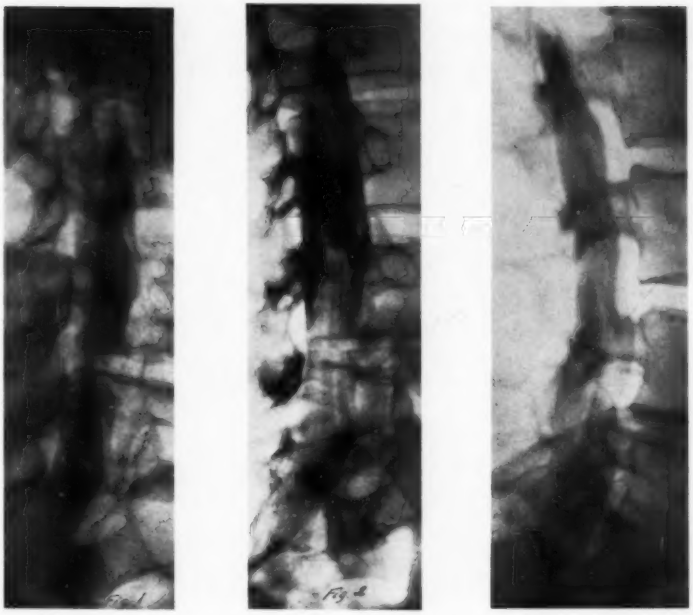
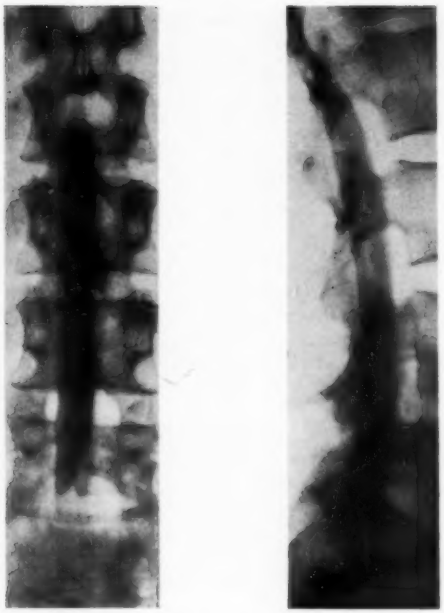


Fig. 1. Myelogram by abrodil showing disk prolapse L_{4-5}.
Figs. 2—3. Same case two months after operation. Myelograms with the abrodil injected both subdurally and subarachnoidally.

cc of 20 percent abrodil had been injected. The complaints of the patients were small, and they disappeared within a few hours.

In the groups 10—11 the complications were manifest spasms in the legs, secondary shock, and paralysis of the legs and sphincters. In all these cases a wrong contrast medium had been injected. The moderate symptoms in the first group appeared after 6—10 cc of 35 percent perabrodil. In the other group 10 cc of 40 percent intron were used. Without any doubt the wrong solutions were responsible for the course and the sequels in these cases.

One case, with two earlier myelographies by abrodil, at a third myelography showed a partial encapsulation of the contrast medium (Figs. 1—3). As was observed in another case the injection may be made subdurally, outside the arachnoid mater, in spite of the fact that spinal fluid drops out of the needle. As a consequence of the subdural deposition the anesthetic effect was less than normal and most of the contrast medium was found on the posterior side of the cauda equina without enclosing



Figs. 4—5. Myelograms by abrodil with all contrast deposited subdurally.

the roots (Figs. 4—5). There is no reason to assume that the encapsulating membrane in the case of repeated myelographies was due to post-arachnoiditic adhesions. Instead, the membrane was the arachnoid mater itself, and the case was not counted as complicated by the previous myelographies.

Conclusions

In order to avoid complications in the myelography by abrodil the following instruction is justified:

A thin needle should be used for the puncture, as a suggestion a needle of 0.5 mm with an introducer for the puncture of the skin and the ligaments.

The patient ought to be prepared against drop in blood pressure. The blood pressure must be controlled, and ephedrin etc. is given when the pressure drops. The head end should be raised only during the examination.

The anestetic solution should not be too heavy. One — two cc of a 5 percent solution of novocain is recommended.

Only approved radiopaque solutions as 20 percent abrodil (or 20 percent intron[1]) should be used. Though there has been no case of anaphylactic reactions in this series allergic tests will ensure safety still better.

In addition to this it must be pointed out that a diagnostic procedure of these proportions should not be performed without a chance of surgical therapy. We know that sciatica is almost the same as disk prolapse, either inside the spinal canal, or inside or lateral to the intervertebral foramina. In the diagnosis of the prolapses the purpose of the myelography is to locate a prolapse in the spinal canal, and this localisation is senseless until operation is indicated.

SUMMARY

A critical examination of reported cases of complications following the myelography by abrodil was made. The complications may be explained by leakage through the puncture canal, by shock on account of the position during lumbal anesthesia, by incomplete anesthesia causing shock and pains, and by wrong opaque solutions. Instructions to avoid complications are given.

ZUSAMMENFASSUNG

Eine kritische Durchsicht der veröffentlichten Fälle von Komplikationen nach Myelographie mit Abrodil. Die Komplikationen lassen sich erklären durch Leckage im Stichkanal, durch Schock infolge der Lage bei der Lumbalanästhesie, durch unvollständige Betäubung, die Schock und Schmerzen gegeben hat, sowie durch falsch bereitete opake Lösungen. Es werden Vorschriften zur Vermeidung von Komplikationen gegeben.

RÉSUMÉ

L'auteur s'est livré à un examen critique des cas où l'on a rapporté des complications à la suite de myélographie à l'Abrodil. Elles peuvent s'expliquer par une perte de liquide à travers l'orifice de ponction, par un shock dû à la position prise pendant la rachianesthésie, par une anesthésie incomplète entraînant du shock et des douleurs, ainsi que par un mauvais choix de la solution opacifiante. Des instructions sont données pour les éviter.

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[1] According to a later report a myelography by 20 percent intron was followed by longstanding pains in the sacral region and paresis of the sphincters.

AUS DER RÖNTGENTECHNISCHEN VERSUCHSANSTALT IN WIEN
(LEITER: DR., DR.-ING. J. ŽAKOVSKY)

Herrn Dr. R. M. Sievert, Stockholm, der die Kondensator-Ionisationskammer zur Messung kurzwelliger Strahlung einführte, zum 50. Geburtstag gewidmet.

EIN NEUES MESSGERÄT FÜR DOSISMESSUNGEN MIT KONDENSATOR-IONISATIONSKAMMERN[1]

von

L. Dörner und *J. Žakovsky*

Sowohl die bisher verwendeten Ladegeräte für Kondensator-Ionisationskammern als auch die zugehörigen Spannungs-Messgeräte weisen Nachteile auf, welche die Verwendung dieses Verfahrens bei Messungen im Bereiche von wenigen Milliröntgen stark einschränken, wenn nicht unmöglich machen. Da diese Grössenordnung zumeist bei Strahlenschutzmessungen vorkommt, gibt die nachstehende Arbeit an, wie durch Verwendung eines neuartigen Ladegerätes mit Sollspannungsmesser[2] und durch Ausnützung einer entsprechend gekrümmten Elektrometer-Kennlinie Messungen mit Kondensator-Ionisationskammern von einigen Milliröntgen bis etwa 1000 Milliröntgen möglich werden, wobei die Messgenauigkeit im ersteren Falle mit einem Fehler von etwa $\pm$ 0.65 mr, im letzteren Falle mit einem solchen von weniger als $\pm$ 2 mr behaftet ist.

I. Das neue Ladegerät mit Sollspannungsmesser

Bei den bisher verwendeten Ladegeräten für Kondensator-Ionisationskammern wird die Spannung mit normalen Betriebs-Messgeräten festgestellt und es hängt daher die Messgenauigkeit von der Klasse des verwendeten Messgerätes ab. Die Ladespannung beträgt bei den für Strahlenschutzmessungen zumeist verwendeten Kondensatorkammern in Zylinderform[3] etwa 400 Volt, der Messbereich höchstens 1000 mr, so dass

[1] Bei der Red. am 15 Aug. 1946 eingegangen.

[2] Als Sollspannungsmesser ist ein Voltmeter bezeichnet, bei welchem nur der engere Bereich um die gewünschte »Soll«-Spannung auf die gesamte Skalenlänge ausgedehnt und der Anfangsbereich unterdrückt ist.

[3] Bezogen von den Physikalisch-technischen Werkstätten, Freiburg/Br., Deutschland.

die Messgenauigkeit $\pm$ 0.2 Volt, gleich 0.05 % von 400 Volt, sein müsste, um im Anfangsbereich auf $\pm$ 0.5 mr genau messen zu können.[1] Nun beträgt diese bei normalen Messgeräten 1 bis 1.5 %.

Es wurden schon verschiedene Versuche unternommen, brauchbare Sollspannungsmesser zu bauen. Am wenigsten befriedigten die mechanischen Lösungen dieses Problems. Eine vor einigen Jahren entwickelte Messbrücke erforderte einen erheblichen Aufwand an Zusatzgeräten. Mit geringerem Aufwand erreichte später eine von Oesinghaus beschriebene[2] Anordnung eine Steigerung der Messgenauigkeit des Instrumentes auf etwa das Zehnfache. Die im Folgenden beschriebene, von den Autoren benutzte Anordnung bedient sich der Strom-Spannungskennlinie von Glimmlampen, um eine möglichst hohe Abhängigkeit der Stromstärke von der Spannung zu erhalten, und erreicht eine Steigerung der Mess-

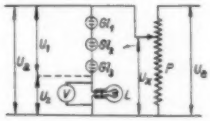

Abb. 1. Prinzipielles Schaltbild des benutzen Sollspannungsmessers.

Es bedeuten U_e = Eingangsspannung (Gleichspannung),
U_x = Vom Potentiometer abgenommene Spannung,
U_1 = Teilspannung an den Glimmlampen,
U_2 = Teilspannung an der Glühlampe,
U_a = Ausgangsspannung, Gl_1, Gl_2, Gl_3 = Glimmlampen
P = Potentiometer, L = Glühlampe, V = Voltmeter.

genauigkeit des verwendeten Voltmeters auf das 25-bis 50-fache. Ausserdem ist das Ladegerät mit einem Sollspannungsmesser zusammengeschaltet, so dass man zur Aufladung der Kammern eine exakt kontrollierte Spannung abnimmt. Da sowohl zur Aufladung der Kammern, wie auch des Elektrometers nur Spannungen und keine Stromstärken benötigt werden, so braucht die Belastung der Glimmlampen nur wenige Milliampere zu betragen.

Von der eingehenden, oberwellenfreien Gleichspannung U_e wird die gewünschte Spannung U_x über ein Potentiometer P abgegriffen und zunächst mehreren in Reihe geschalteten Glimmlampen Gl_1, Gl_2, Gl_3 zu-

[1] Dabei sind die weiteren Fehlerquellen bei der Dosismessung, die durch Welligkeit der Ladespanung, Kontaktpotentiale bei Ladung und Messung der Kammer, Ablesegenauigkeit des Elektrometers, Konstanz der Elektrometereichung und der Kammer-Konstanten, die sich gerade bei Messungen im Bereiche von wenigen Milliröntgen am meisten auswirken, unberücksichtigt gelassen, so dass Messungen unterhalb 25 mr, der höchstzulässigen Tagesdosis, recht wenig brauchbare Werte erwarten lassen.

[2] W. Oesinghaus, Der neue Sollspannungsmesser, ETZ 65. Jg. (1944), H 3/4, S. 33.

geführt. In Reihe mit den Glimmlampen befindet sich ein Widerstand L, dessen Strom-Spannungs-Kennlinie geringe Steilheit aufweist und dessen Widerstandswert im Verhältnis zu jenem der Glimmlampen gering sein muss, wie es bei einer bei etwa 1 bis 2 % der Nennspannung arbeitenden Metallfadenlampe der Fall ist. Parallel zu ihr liegt das Anzeigevoltmeter V, dessen Widerstandswert der Drehspule so hoch sein muss, dass für die Stromstärke im Instrument lediglich der Spannungsabfall an der Metallfadenlampe bestimmend ist. Unter diesen Voraussetzungen teilt sich die Spannung U_x in die Teilspannung an den Glimmlampen U_1 und jene an der Metallfadenlampe U_2, wobei $U_2 \ll U_1$ und proportional U_x ist.

Das Zusammenwirken der Strom-Spannungs-Kennlinie der Glimmlampen mit jener der Metallfadenlampe zeigt Abbildung 2. Die rechte Kurve dieser Abbildung zeigt die Kennlinie der Glimmlampen; auf der Abszisse ist die zu messende Spannung U_x in Prozenten vom Sollwert, auf der Ordinate die Glimmlampen und Metallfadenlampe gemeinsam durchfliessende Stromstärke J aufgetragen. Die linke Kurve zeigt die Kennlinie der Metallfadenlampe im Spiegelbild; auf der Abszisse nach links ist das Skalenbild des an der Metallfadenlampe liegenden Voltmeters aufgetragen. Bei der eingezeichneten Kennlinie der Glimmlampen bewirkt eine Änderung der zu messenden Spannung U_x von 99 auf 101 % eine Änderung der Stromstärke von 5 auf 8 mA in den Glimmlampen und damit auch in der Metallfadenlampe. Infolge der geringen Steilheit der Kennlinie der Metallfadenlampe hat diese Stromstärkenänderung von 3 mA eine grosse Spannungsänderung an der Lampe zur Folge. Der besseren Anschaulichkeit halber sind die Verhältnisse in der Abbildung für die Skalenmitte (50 Skalenteile gleich 100 % Sollspannung) durchgezeichnet. Es ergibt sich dann, wie die linke Kurve zeigt, für 3 mA Stromstärkenänderung eine Änderung von 29 auf 80, also von 51 Skalenteilen am Anzeigeinstrument. Somit wurde das Intervall von 99 bis 101 %, beziehungsweise ± 1 % der zu messenden Spannung auf den Bereich von 51 Skalenteilen um den Mittelwert von 50 Skalenteilen herum erstreckt. Da die Messgenauigkeit eines Instrumentes im Bereiche der Skalenmitte nur den halben Wert beträgt, so wurde im gezeigten Falle die Messgenauigkeit auf das 25-fache gesteigert. Wenn man unter sonst gleichen Umständen den Instrumentenausschlag von der Skalenmitte an das Skalenende verlegt, erhält man 50-fache Messgenauigkeit.

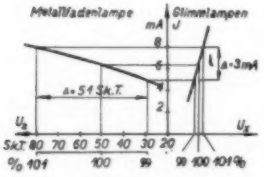

Abb. 2. Zusammenwirken der Strom-Spannungs-Kennlinie der Glimmlampen mit der Strom-Spannungs-Kennlinie der Metallfadenlampe.

II. Die Kennlinie des Elektrometers

Infolge ihrer Vorteile setzen sich bei elektrischen Schaltanordnungen Schaltelemente, deren Funktionswert in exponentieller an Stelle der früher üblichen, linearen Abhängigkeit von der mechanischen Verstellung abhängt, immer mehr durch. Es sei nur auf die Drehkondensatoren mit logarithmischer Skalenteilung in der Radiotechnik und auf die Schaltuhren mit logaritmischer Skala bei Röntgenapparaten verwiesen. Es lag daher nahe, diesen Vorteil für die Messung der durch die Entladung bewirkten Spannungsdifferenz, welche proportional der gesuchten Dosis ist, auszunützen.

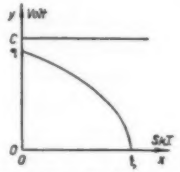

Abb. 3. Eichkurve eines Einfaden-Elektrometers ohne Hilfsspannung.

Es bedeuten x = Ausschlag des Elektrometers in Skalenteilen,
y = Spannung am Elektrometer in Volt,
ξ = Maximalwert des verwendeten Skalenbereiches,
η = Maximalspannung im verwendeten Skalenbereiche,
C = Konstante, z. B. maximale Messspannung des Elektrometers.

Wenn die Zunahme der Spannungsdifferenz an jeder Stelle der Eichkurve proportional dem Wert der Spannungsdifferenz sein soll, in welchem Falle gleicher prozentualer Fehler im ganzen Messbereich erhalten wird, so muss gelten

$$\frac{dy}{dx} = -\beta\,(C - y).$$ Es bedeuten β = Proportionalitetsfaktor, C = Konstante

Die Lösung dieser Differentialgleichung mit den Zusatzbedingungen

$x = 0,\ y = \eta$ und
$x = \xi,\ y = 0$

lautet

$$y = C\,(1 - e^{\beta x'})$$

$$\text{mit } C = \frac{\eta}{1 - e^{-\beta\xi}} = \text{Konstante}$$

$$x' = x - \xi$$

Da die Eichkurve des Elektrometers ohne Hilfsspannung eine ähnliche Krümmung, wie sie die obige Gleichung fordert, aufweist, wurde

untersucht, inwieweit die Eichkurve von einer durch die Skalenpunkte 0, 50 und 100 approximierten Exponentialkurve abweicht.

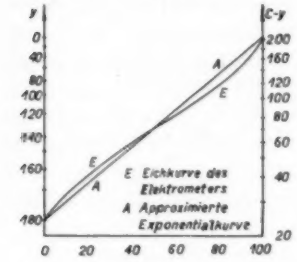

Abb. 4. Vergleich der Eichkurve des Elektrometers ohne Hilfsspannung mit der approximierten Exponentialkurve, die gleichen prozentualen Fehler im ganzen Messbereich ergibt.

Aus den Ordinaten der drei Punkte

$$y_{x=0} = 180, \quad y_{x=50} = 134, \quad y_{x=100} = 0$$

konnten leicht die Zahlenwerte für

$$\beta = 0.02138 \text{ und } C = 204.05$$

bestimmt werden.

Die Unterschiede zwischen den beiden Kurven sind in Abbildung 4 zum Vergleich gegenübergestellt, wobei aus Zweckmässigkeitsgründen für die Darstellung der Ordinaten ein logarithmischer Massstab angewendet wurde.

Man ersieht aus Abb. 4, dass die Anwendung einer gekrümmten Eichkurve, die nur im Anfangsberecih der Kurve um mehr als 20 % von der approximierten Exponentialkurve abweicht, den Vorteil bietet, im ganzen Messbereich mit fast gleicher Messgenauigkeit die Dosismessungen ausführen zu können.

III. Durchführung der Messungen

Zunächst benötigt die Messanlage infolge der Verwendung von Glimmlampen eine gewisse Einlaufzeit. Diese beträgt nach durchgeführten Kontrollmessungen 100 Sekunden. Im Augenblick der Zündung erreicht die Spannung 98.7 %, und 60 Sekunden später 99.9 % ihres Sollwertes von 400 Volt. Hierauf wird die Eichkurve des Elektrometers nachgeprüft, worauf die Aufladung der Kammer unter Kontrolle am Elektrometer erfolgt. Nun kann die Kammer am Messort der Strahlung ausgesetzt werden. Zur Bestimmung der Restladung der Kammer wird die Eichkurve des Elektrometers neuerlich nachgeprüft und sodann nach Aufsetzen der Kammer ihre Spannung mittels des Elektrometer-Ausschlages gemessen. Die so erhaltene Spannungsdifferenz, multipliziert mit der Eichkonstanten der Kammer in Milliröntgen pro Volt, ergibt die der Kammer verabreichte Dosis in Milliröntgen.

IV. Fehler des Messwerfahrens

Zur Bestimmung des Gesamtfehlers war es notwendig, die Einzelfehler des Verfahrens zu bestimmen. Bei Verlegung des Instrumenten-

ausschlages an das Skalenende ergaben sich die nachstehenden Verhältnisse.

1 Einstellgenauigkeit der Ladespannung mittels des Sollspannungsmessers nach einer Einlaufzeit von 100 Sekunden $400\,V \cdot \pm 1\,\% \cdot \frac{1}{50}$	$\pm$ 0.08 V	$\pm$ 0.08 V
2 Welligkeit der abgegebenen Spannung mittels Anzeigeinstrument bestimmt zu	$\pm$ 0.1 V	$\pm$ 0.1 V
3 Genauigkeit der Messung der Kammerspannung mittels Elektrometer, bestimmt für $\pm$ 0.1 Skalenteil Ablesegenauigkeit und bezogen auf die Ladespannung von 400 Volt		
a) im Bereiche von 400 Volt, entsprechend Dosiswerten von wenigen Milliröntgen	$\pm$ 0.08 V	
b) im Bereiche von 100 Volt, entsprechend Dosiswerten bis zu 1000 Milliröntgen		$\pm$ 0.56 V
	$\pm$ 0.26 V	$\pm$ 0.74 V

Regelmässig durchgeführte Kontrollen in einer Dauer von mehr als drei Monaten haben im Bereiche von 400 Volt Kammerspannung einen Messfehler von nicht mehr als $\pm$ 0.3 Volt ergeben. Somit kann der Messfehler im Bereiche von 400 V Kammerspannung, dessen man sich bei Messung kleiner Milliröntgen-Werte bedient, mit $\pm$ 0.65 mr und jener im Bereiche von 100 V Kammerspannung, der bei Messung von Dosen bis zu 1000 Milliröntgen benützt wird, mit weniger als $\pm$ 2 mr angesetzt werden.

ZUSAMMENFASSUNG

Es wird ein neues Messgerät für Dosismessungen mit Kondensator-Ionisationskammern beschrieben. Dieses bedient sich zum ersten Male der Glimmlampen für die Schaltung eines Sollspannungsmessers und verwendet ein Einfaden-Elektrometer ohne Hilfsspannung, um die Vorteile der dabei einer Exponentialkurve ähnelnden Eichkurve ausnützen zu können. Im Bereiche von wenigen Milliröntgen kann damit die Dosis mit einem Fehler von $\pm$ 0.65 mr, im Bereiche bis zu 1000 Milliröntgen mit einem solchen von weniger als $\pm$ 2 mr bestimmt werden.

SUMMARY

A description is given of a new dosimetric meter with condenser ionisation chambers. For the first time this is used with gas-filled lamps for switching with a blade-type switch and for single wire electrometer without auxiliary tension so as to be able thereby to make use of a rectifying curve similar to an exponential curve. The dose can be determined within a range of a few mr with a margin of $\pm$ 0.65 mr and within a range of up to 1000 mr with a similar margin of $\pm$ 2 mr.

RÉSUMÉ

Description d'un nouvel appareil de mesure pour la dosimétrie par cellules d'ionisation à condensateur. Cet appareil utilise pour la première fois les lampes veilleuses pour enclancher un commutateur de mesure de la tension brute, et se sert d'un électromètre à fil unique sans tension de secours afin de profiter des avantages de la courbe exponentielle, qui dans ce cas ressemble à une courbe d'étalonnage. Lorsqu'on travaille avec seulement quelques milliroentgens la dose peut ainsi être déterminée avec une marge d'erreur de $\pm$ 0.65 mr., et quand on va jusqu'à 1000 milliroentgens cette marge est inférieure à $\pm$ 2 mr.

FROM THE ROENTGEN CLINIC OF THE AARHUS MUNICIPAL HOSPITAL AND THE RADIUM CENTER FOR JUTLAND, DENMARK (CHIEF: PROF. CARL KREBS, M. D.)

MEDIASTINAL TUMORS IN LEUKOSIS[1]

by

Jørgen Bichel

In the last fifteen years, 217 patients with leukosis have been treated at the Radium Center for Jutland. Fifty-three of the cases were chronic myeloid, 129 chronic lymphatic, 22 acute; the rest (13) either more uncommon forms or the diagnosis was uncertain. At present writing (Nov. 1945), 39 of the patients are still alive, 9 with chronic myeloid, 30 with chronic lymphatic leukosis.

Most of the patients were regularly roentgen-examined with a view to possible changes in the mediastinum and lungs, and also in those who died and came to necropsy such changes were particularly looked for. No sure signs of mediastinal changes were found in any of the chronic myeloid cases, but in the chronic lymphatic it was rather usual on roentgen examination to find some enlargement of the hilus region, from doubtful increase of the opacity to larger, coronally defined or round, circumscribed lymph node shadows of varying size, as elements of a general swelling of the glands. They only in a few instances attained the size of a hen's egg, though, and rarely gave any symptoms, therefore also seldom indication for treatment.

Among the patients with acute leukosis, there were four in whom mediastinal tumors were found, probably arising from the thymus. In two of them, this tumor was the absolutely dominating symptom at admission. These four cases are related in the following and discussed in connexion with similar cases from the literature.

Case I. — Male, 21 years old; farmhand, single. Admitted Apr. 2nd, 1937 (no. 519/37). Paternal grandfather said to have had acromegalia, otherwise nothing relevant in the family history. Two and a half months before admission, the patient got »influenza», accesses of fever, and a few weeks after his face began to get swollen, but he did not feel ill. In short time the swelling spread downwards to the neck and thorax, then there were slight attacks of suffocation, stridulous respiration and coughing, but no expectoration.

[1] Submitted for publication, June 6, 1946. Aided by a grant from the Anders Hasselbalch Anti-Leukemia Foundation.

He kept his bed, but the tumefaction increased and he began to feel tired. At admission, his appearance was that of a young man much worn out, but in normal state of nutrition. There was marked edema of the whole face and down over the neck, the arms and the upper part of the thorax. The face, moreover, was highly cyanotic, the eyes »bloodshot» and watering. He sat up in bed, extremely dyspneic; the respiration was rasping. Palpation showed general swelling of the lymph glands, which were from bean- to hazelnut-sized; the liver and spleen did not feel enlarged. There was marked phlebectasia over the thorax. Roentgenography showed an immense tumor of the mediastinum (Fig. 1), bulging largely to both sides, with clean demarcation from the lung tissue. Downwards on the right side there was strong blurring. The patient was slightly febrile. There was no albumen, pus or sugar in the urine. Wassermann, negative. About blood examinations and sternal puncture, see below.

Cautious roentgen treatment of the large mediastinal tumor was instituted, over two anterior and two posterior fields, only to one field each day. Dose at each sitting, 50 r through 1 mm. Al + 1 mm. Cu (160 kv., 4 ma., distance 40 cm.). There were no untoward reactions; on the contrary, the patient began to feel better, the dyspnea, cyanosis and edema diminished, and after 100 r, in all, had been given to each of the four fields it was found that the mediastinal tumor had almost completely disappeared (Fig. 2). The patient felt perfectly well, and on May 1st, a month after admission, he could be discharged.

For some weeks he remained at home, feeling all right, but then he again became dyspneic, and now also got pains across the abdomen. On May 18th, he was re-admitted, presenting the same symptoms as at first admission, though in a milder degree. But there was now also tumefaction of the liver and spleen, which both could be felt three to four fingers' breadth below the costal margin, and besides there was some ascites. Roentgen examination of the thorax showed incipient reproduction of the mediastinal tumor and signs of exudate in the right side. A liter and a half of slightly bloody fluid was evacuated by pleural puncture. The patient rapidly got weaker, the dyspnea, edema and cyanosis increased. The temperature rose to about 39° C., he became somnolent, and on June 7th, 1937, he died. In the last days before death there was incipient gingivitis, but no signs of hemorrhagic diathesis.

Blood examination:

	Apr. 3rd	Apr. 5th	Apr. 15th	May 1st	May 19th	May 22nd	May 25th	June 3rd
Sedimentation	17			24	54			
Hemoglobin		78	75	93	40	33	26	12
Red cells		3.18	3.50	4.00	1.37	1.15	1.00	0.55
White cells		4,800	7,000	16,000	14,300	8,600	5,500	3,000
Blasts		24	25	68	98.3		100	
Myelocytes, neutrophil		7.5	3	0.5	0.3			
Metamyelocytes		3.5	1.5					
Polymorphonuclear, neutrophil		31.5	43	9	0.6			
» eosinophil		1.5						
» basophil			0.5					
Lymphocytes		31	22	21.5	0.6			
Monocytes		1	5	1				
Normoblasts		8/200	4/200	4/200	5/300			
Thrombocytes					62,000			

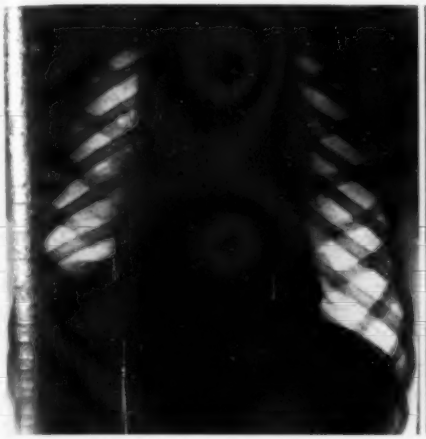

Fig. 1.

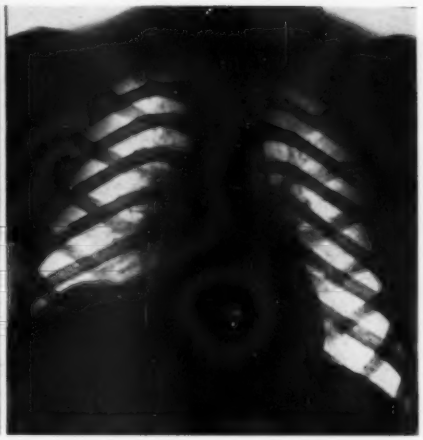

Fig. 2.

The cells described as blasts were round cells, from 10 to about 22 μ in diameter, with round or slightly kidney-shaped, rather immature-looking nuclei of delicate, slightly granular structure and with two or three distinct nucleoles. The cytoplasm was highly basophil, non-granular, with a clear zone surrounding the nucleus and with more or less distinct cytocentrum. It was very scant, oftenest seen only as a very narrow border about the large nucleus, which in many places seemed entirely uncovered. Its oxydase reaction was negative. Some of the cells were somewhat smaller; possibly a few have been listed as lymphocytes. In the preparations, a few cells were seen sending out small processes from the cytoplasm. Sternal puncture was done on April 17th. The fluid withdrawn was rich in cells (440,000 per cubic millimeter), with blasts 81.3 per cent, neutrophil myelocytes 1.3 per cent, metamyelocytes 0.3 per cent, normoblasts 14.6 per cent, larger immature precursory stages of erythrocytes 2.3 per cent. The blasts were of the same appearance as those in the blood.

On April 20th, pleural puncture was done on the right side, in the eighth costal interspace, and 1.5 liter of slightly bloody fluid evacuated, which contained 20,000 nucleated cells per cubic millimeter, almost exclusively blasts as those described above.

The necropsy, on June 8th, revealed at the site of the thymus a cylindric tumor 12 cm. long and 4—5 cm. in diameter, firm, with slightly buckled surface, well marked off from the lung tissue, but adhering to the pericardium. The right pleural cavity contained 2 liters of serous fluid. Over both pleurae there was a scattering of pinhead-sized, greyish-white nodules. The peritoneum contained 0.5 liter of serous fluid. The spleen weighed 350 grams and measured 16 × 10 cm. The section surface showed a number of a little less than pinhead-sized, white nodules disseminated through the parenchyma. The liver measured 33 by 20 cm., the edges were plump, the surface smooth, there were no distinct leukemic infiltrates on the section surfaces. The kidneys measured 12 × 6 cm., the capsules were readily detachable. In the pale parenchyma, there were white infiltrates both on the surface and the section surfaces. Both in the hilus of the lungs, along the aorta, in the porta hepatis and in the mesentery there were lymph glands from walnut- to apple-sized, all of rather firm consistence, with hemorrhagic section surfaces, but without

necroses. Histologically, the large mediastinal tumor was composed of large, closely set round cells of the same type as the blasts, already described, in the blood. In between the compact tumor tissue were seen remnants of the thymus tissue in the form of Hassall's corpuscles. In the spleen, the follicular structure was completely effaced by a diffuse round-cell infiltration. Also in the liver, about the portal veins., there were round-cell infiltrates. In the kidneys there were infiltrates both perivascular and diffuse and between the tubules.

Epicrisis. — A man, 21 years old, was admitted, with edema of the face, dyspnea, cyanosis and attacks of suffocation, due to a large mediastinal tumor. Examination of the blood showed, of 4,800 white corpuscles, 24 per cent very immature (»blasts»). The mediastinal tumor proved extremely radiosensitive, and disappeared almost completely after a small dose of roentgen. At the same time, the patient's symptoms disappeared, and he was discharged. Seventeen days after, he returned and was re-admitted. The mediastinal tumor had partly reproduced itself, and besides there was now tumefaction of the liver and spleen, and general swelling of the lymph glands. Moreover, profound anemia had developed; of 14,300 white cells, 98 per cent were »blasts». Already at the first admission, the same immature cells had been found disseminated in the bone marrow and in a right-side pleural exudate. There came slight symptoms from the cavity of the mouth and the patient died. Though at one examination thrombopenia was demonstrated, there was no hemorrhagic diathesis.

Case II. — Male, 19 years old, single. Dairy apprentice. Admitted May 31st, 1945 (no. 1091/45). Family history, nothing relevant. In April 1945, the patient noticed a developing swelling on the right side of his neck. There had been no preceding illness. The swelling increased rapidly, and he was admitted to a hospital in another town, where a biopsy was performed and the case diagnosed as lymphosarcoma. He was therefore transferred to the Radium Center in Aarhus, for radiation treatment. At admission here, he stated that he had not been feeling ill until in the last few days. The tumor in the neck had not been tender to the touch, and had not caused him any discomfort. In the last days he had become more and more short of breath, and the respiration had now become so difficult that he could only get along by sitting up in bed. Apart from the dyspnea and a little »tenderness» in the neck he had no complaints. At admission here, his appearance was that of a well built young man in a state of nutrition somewhat below the normal. The difficulty of breathing gave him a great deal of trouble, he had to sit up in bed, and his respiration was rasping and wheezing. There was some cyanosis of the lips, slight edema of the whole face and down over the neck, and marked phlebectasia over the upper part of the chest. The left side of the neck and supraclavicular region was the seat of a smooth, firm, indolent tumor, the size of a coconut. The skin over it was movable and natural. Besides, there were a few hazelnut-sized glands on both sides of the neck and in the axillae. There was no palpable enlargement of the liver or spleen. In various parts of the body there were a few petechiae. There was some redness in the fauces, and incipient gingivitis with some bleeding at the neck of the teeth. Roentgen examination of the thorax showed a large mediastinal tumor, mainly situated in the superior and anterior portions of the latter. It was sharply marked off from the lung tissue, with smooth edges, and measured at its broadest part 14 centimeters.

At admission, the patient was slightly feverish, and during his entire stay his temperature stood about 38° C. No sugar or albumin in the urine. Wassermann, negative. About blood examinations, sternal- and lymph-gland punctures, see below.

Roentgen treatment of the large mediastinal tumor was instituted, with irradiation over two posterior fields, later one anterior field; 25 to 35 r daily through 1 mm. Al + 1 mm. Cu (160 kv., 4 ma., distance 40 cm.); total to each of the three fields respectively 21, 25 and 175 r. Thereafter 200 r, in all, to each of two fields over the tumor in the left side of the neck. Besides, calcii glyconatis tablets were given, 0.5 g. six times daily. The treatment soon relieved the patient's condition somewhat; the dyspnea lessened, so that he could lie down in bed; but neither the mediastinal tumor nor the tumor in the neck became very much smaller. A hemorrhagic diathesis developed, with numerous petechiae all over the body and strong bleeding from the gums. The patient got weaker and weaker, in spite of blood transfusions a rapidly progredient anemia developed. After his own wish he was discharged on July 17th, and on July 20th he died at home.

Blood examination:

	June 1st	June 4th	June 8th	June 12th	June 15th	June 22nd	June 26th	July 6th	July 13th
Sedimentation	10	11	16	15	15	17	16	20	20
Hemoglobin	105	110	102	106	106	96	83	64	45
Red cells	4.62	4.59	4.13	4.73	4.76	3.76	3.17	2.56	2.05
White cells	7,600	13,000	25,000	49,000	108,000	110,000	118,000	83,000	76,000
Blasts	1	5	8	59.5			89.5	82	99
Myelocytes, neutrophil	1	2	5	1			1	3	
Metamyelocytes	1	2	8	4			2.5		
Polymorphonuclear, neutrophil	49	59	56	15			4	5	1
Polymorphonuclear, eosinophil		2	3	1.5					
Lymphocytes	43	20	10	15			3	10	
Monocytes	5	10	10	4					
Normoblasts				1/200			1/200		
Thrombocytes		400,000					8,000		

The cells listed as »blasts» were round cells from about 8 to about 20 μ in diameter, with delicately structured round or kidney-shaped, sometimes lobed nuclei, and some of them with two distinct nucleoles. The nucleus filled almost the entire cell, so that the cytoplasm was only seen as a narrow rim, often with a clear zone about the nucleus. The oxydase reaction of the cells was negative. A number of »shadows» were seen in all the preparations. Sternal puncture (July 4th) yielded a fluid rich in cells, nearly all large, immature, of the same type as the blasts in the blood, and likewise oxydase-negative. At the same time, a puncture was done of the gland in the left side of the neck. Also here the fluid withdrawn was rich in cells and showed a pure culture of the blasts described above.

Epicrisis. — In a young man, 19 years old, a tumor developed in the left side of the neck, without preceding illness. Microscopy showed lymphosarcoma. Shortly after, respiratory trouble set in, there came edema of the face and cyanosis, and it was found that the patient had a

large mediastinal tumor. Blood examination showed 7,600 white corpuscles, with a few very immature cells. Roentgen treatment resulted in some improvement of his condition, but immediately afterwards a hemorrhagic diathesis developed; the blood picture showing increasing lymphocyte values, with rapidly increasing number of very immature cells and progressive anemia, and the patient died with symptoms as in acute leukemia.

Case III. — Female, 4 years old (no. 2918/44), admitted Nov. 14th, 1944, with acute lymphatic leukosis. Her paternal grandfather had died of chronic lymphatic leukosis, otherwise nothing relevant in the family history. According to the information given she had not been a particularly sickly child, except for some disposition to catarrhs. A blood examination in 1943, when she was hospitalised for angina, had not shown anything abnormal; it appears, though, that she always had had some slight glandular swellings in the neck, and that these had become a little larger in the last three months. In August 1944, she had one night suddenly got a severe pain in the abdomen. It soon disappeared, but her temperature had remained at about 38—39° C. In September 1944, she had been admitted to another hospital, where her case was diagnosed as lymphatic leukosis. Since then, her condition seems to have been somewhat up and down, but on the whole she had been falling off. Her temperature remained rather high, and she had begun to suffer from nosebleeds. She had been given blood transfusions and had been treated with arsenic.

At admission to the Radium Center, Nov. 14th, 1944, her condition was nevertheless tolerably good. She was pale, but with feverishly flushed cheeks; her nutritional state was somewhat below medium, and she was rather enfeebled. In the parotic region, there were on both sides pigeon-egg-sized, firm, indolent intumescences; in both sides of the neck, in the axillae and the groin bean-sized glands. The spleen could be felt one to two fingers' breadth below the costal margin, its border was not tender to the touch. There was no enlargement of the liver. Otherwise there was nothing to remark at objective examination. There was no sugar or albumen in the urine. The diastase values in the latter were normal. Roentgen examination of the lungs showed a moderate increase in the breadth of the mediastinum shadow in the anterior and superior portions of the latter, most pronounced on the right side, where the contour was seen smooth and sharply marked off against the lung tissue.

Blood examination:

	Nov. 16th	Nov. 21st	Nov. 25th	Dec. 1st	Dec. 5th	Dec. 8th	Dec. 12th	Dec. 15th
Hemoglobin	96	92	96	86	86	62	43	29
Red cells	5.43	6.10	4.91	4.56	3.93	3.87	2.36	1.49
White cells	20,800	20,800	17,100	21,200	13,400	5,200	4,700	800
Polymorphonuclear, neutrophil	21		15	6	5		3	19
» eosinophil								
Lymphocytes	79		85	94	95		97	81

Most of the lymphocytes were rather atypical cells. They were about twice as large as normal lymphocytes, and the deviation from type showed itself particularly in the way in which the nucleus filled the whole cell, so that the cytoplasm in many cases could

practically only be seen where there, as in many of them, were small indentations in the nucleus. The chromatin lay in bits and heaps. Only in a few cells could a distinct nucleolus be seen. The cytoplasm was agranular and slightly basophil. Larger cells of pronounced plastic type were rare. Besides these atypical cells, there were normal lymphocytes of the medium-sized type, with abundant cytoplasm and azurophil granules. In most of the preparations, some shadows were seen; very seldom a nucleated erythrocyte or a myelocyte.

Cautious roentgen treatment of the tumors in the parotic region was instituted, but the patient soon went downhill. Suppurating otitis media developed on the left side, she got violent nosebleeds, and despite blood transfusions she died Dec. 17th, 1944.

A partial necropsy revealed enlargement of the glands in the mesentery and mediastinum, considerable enlargement of the thymus and moderate enlargement of the liver, spleen and kidneys. Histologic examination showed that the coarser structure of the lymph glands was preserved, but the follicular design effaced, and no germinal centers were seen. In the reticular supporting tissue there was a uniformely diffuse accumulation of large and small lymphocytes. In the bone marrow there was a massive infiltration of lymphocytes of various size. The myelopoiesis was suppressed. The spleen was extremely congested; the coarser structure was intact, but no follicles or germinal centers were seen; on the other hand there were in many places large accumulations of lymphocytes. Also in the liver there were large masses of lymphocytes, both in the portal chambers and, to varying extent, in the sinusoids. In the kidneys, the lymphocyte infiltration was so immense that the tubules and collecting tubes lay burst far apart from each other by their accumulation.

Epicrisis. — In a girl, 4 years old, lymphatic leukosis was diagnosed after she had for a short time been showing symptoms of fever. In the course of the disease, Mikulicz's syndrome developed, there was general swelling of the lymph glands, tumefaction of the liver and spleen, and enlargement of the thymus. She was given blood transfusions and treated with arsenic and roentgen, but an increasing hemorrhagic diathesis and, finally, suppurating otitis media set in, and after being ill for four or five months she died.

The fourth case has already been published by KNUD HØYER, and is therefore only briefly summarised here.

Case IV. — A boy, 8 years old (no. 618/41), was taken ill with fever and a bullous dermatitis, which healed, leaving pigmentations. Two months later, cough, fever and pain in the abdomen set in. At admission, three months after the onset of the disease, there was swelling of the lymph glands, liver and spleen, and blood examination showed lymphatic leukosis. A few days later he suddenly became unconscious, with symptoms from the meninges, suspended patellar reflexes and bilateral Babinski. After three or four attacks of tonic convulsion he died. Necropsy showed changes characteristic of acute lymphatic leukosis. The brain was large, edematous, and throughout it there were numerous minute hemorrhages, which under the microscope proved to be due to perivascular infiltration of lymphocytes. The thymus was much enlarged, weighed 225 grams and adhered to the pericardium. Histologically, it appeared as a meshwork filled with lymphocytes, without any positive trace of Hassall's corpuscles.

Discussion

The first of the cases here described belongs to the type which STERNBERG calls leukosarcomatosis, by which he understands the condition which exists when a lymphosarcoma is associated with leukemic blood picture. Case II is undoubtedly of the same type, though it cannot be affirmed with absolute certainty, since necropsy with examination of the organs was not performed. It is not my intention here to discuss the question whether or not leukosarcomatosis should rightly be considered as a pathologic entity, different on the one side from lymphosarcomatosis, on the other from lymphatic leukosis; — a question which we may believe will be answered when some day the problem of the relation of leukotic processes to tumors in man shall have found its solution. The association of a mediastinal tumor with a leukemic blood picture has often attracted attention, and cases of this character have been set up as a special group; which at any rate from the clinical point of view is justified, since they as a rule differ, both in symptoms, course and prognosis, as well from other mediastinal tumors as from most leukoses. COOK, in 1932, collected 74 such cases, and added to them 9 observed by himself. I have succeeded in finding 33 more, chiefly from the more recent literature, and been able to add 3 of my own observation. In all these 119 cases except one, it has been possible to get the age at onset of the disease ascertained. As it clearly appears from Table I and the curve Fig. 1, it is most frequent in children.

Table I.

Age (years).	Male.	Female.	Unknown.	Total.
0—4	6	4	2	12
5—9	28	7	1	36
10—14	16	1	0	17
15—19	10	3	0	13
20—24	18	0	0	18
25—29	7	1	1	9
30—34	1	1	0	2
35—39	3	2	0	5
40—44	2	1	0	3
45—49	1	0	0	1
50—54	0	0	0	0
55—59	0	0	0	0
60—64	2	0	0	2
				118

The sex could be ascertained in 114 of the cases; the preponderance of males was considerable, namely 95 males to 19 females. The corresponding figures for COOK's material were respectively 68 and 12.

A few authors (ENGELBRECHT-HOLM, among others) believe that they have observed seasonal variations in the incidence of leukosis. I have therefore examined if any such variations could be demonstrated in the present material. It is, of course, extremely difficult, though, to arrive at any definite conclusion on this point, because the initial symptoms in many cases are rather vague. Statements capable of being used for such an examination are found with respect to the first appearance of symptoms in 55 cases, with respect to the month of admission to hospital in 61. As it will be seen from Table II, the cases are fairly evenly distributed over the whole year.

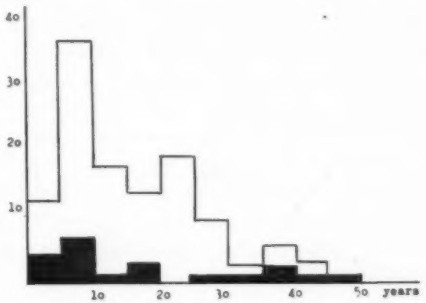

Fig. 3.

Table II.

	Jan.	Feb.	March	Apr.	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.	
First appearance of symptoms . . .	5	6	2	7	5	2	4	6	2	7	4	6	56
Admission to hospital	3	5	6	4	4	2	9	3	6	5	7	8	62

The initial symptoms differ from those of both acute and chronic leukoses in so far as they in the great majority of cases are referable to the large mediastinal tumor in the nature of increasing dyspnea, cough, labored, stridulous respiration and attacks of suffocation, so that the patient often only can manage by sitting up in bed. Cyanosis, edema of the face, neck and arms, bloodshot eyes (sometimes right-side Horner's syndrome) and phlebectasia on the upper part of the body are frequent, and are all readily accounted for by the presence of the intrathoracic tumor. In many cases, the latter is readily demonstrable by objective examination, or at any rate by roentgen examination, and is often accompanied by a bloody, serous exudate, oftenest on the left side. The tumors are extremely radiosensitive. The instituted roentgen treatment will nearly always cause a miraculous improvement in the patient's condition, all the symptoms due to pressure from the tumor disappearing, often in the course of only a few days. But shortly afterwards signs of acute leukosis develop, often with marked hemorrhagic diathesis, and the patient rapidly succumbs.

When the patient enters the hospital, it will therefore oftenest be the mediastinal tumor that dominates the picture, and only after the latter has disappeared, or, at any rate, has diminished considerably, and the patient to all appearances has improved considerably and often has become entirely symptom-free, do the symptoms of acute leukosis develop and speedily lead to the fatal issue.

The mediastinal tumor is usually very large and is always described as situated in the anterior portion of the mediastinum, oftenest in the upper part of the latter, and often of exterior configuration like a thymus. Glandular swelling is a finding which varies considerably. At the first examination there may be none at all, or there may be a more or less general or local swelling of the glands; the most frequent seems to be that in the late stages of the disease there comes a rapidly increasing swelling of the lymph nodes, and the same applies to the enlargement of the liver and spleen.

The hematologic features are very interesting, but are not yet fully elucidated. There is hardly any doubt, though, that quite a number of cases have been observed in which the blood picture in the beginning was perfectly normal, but later became acute leukemic — remarkably often in direct sequel to the irradiation therapy. With regard to some of these investigations, some reservation is necessary, however; because it must be considered as very difficult, especially in the case of children, to determine exactly *when* a normal blood picture changes in to an aleukemic lymphatic. On the other hand, it should be rather easy to determine in the cases in which the typical »leukosarcoma cell» is the dominating type. At any rate it is certain, though, that many of these cases in the beginning show a stable, to all appearances normal leukocyte picture, and then rather suddenly develop a rapidly increasing leukemic blood picture. In the last days of the disease, there is often a considerable fall in the leukocyte values, and in the preparations one then sees almost exclusively the immature, abnormal cells. Corresponding to this development, the hemoglobin percentage and the erythrocyte values are often normal at the first examination (or even increased, owing to the oxygen shortage), and then suddenly drop rapidly, simultaneously with the development of the leukemic blood picture and the hemorrhagic diathesis. Thrombocyte counts have only been made in a few instances, but at any rate thrombopenia has often been observed in the last stages. The same immature and atypical cells as in the blood stream are found as diffuse or circumscribed infiltrates in the different organs, especially in the blood, marrow, liver, spleen, lymph glands and — noticeably often — in the kidneys. Their extension and aggressiveness in the different cases and, in the individual case, in the different organs, is extremely various. Any sure estimate of whether the leukosis is of leukemic or myeloid character

as not yet been reached. From the study of all these cases, one gets the impression that the mediastinal tumor in many of them has existed for some time as an isolated affection, whereupon there suddenly has occurred an emigration of these tumor cells into the blood stream, causing the acute leukosis. In future cases, the modern methods for intravital investigation of bone marrow and hematopoietic and other organs should be employed in order to get a clearer light on these matters, which are of great theoretic interest. In that connexion, it is less important whether the already established condition in the organs is of more circumscribed, infiltrative or diffuse character. All these forms are found, often side by side. It has often been discussed from which organ the »primary» tumor arose. Since it is nearly always found at the site of, and has the same configuration as, the thymus, and on histologic examination is often found to contain remnants of the latter in the form of Hassall's corpuscles, it is generally believed that it arises from that organ. What also adds support to this view is the age distribution, which shows that the overwhelming majority of cases occur in the age classes where the thymus still is abundant. Moreover, it seems to me significant that even in the cases in which no thymus remnants could be demonstrated there is never any mention of the gland itself having been present, though this should certainly be the case in many children. There has been considerable discussion of whether the tumor arose as result of the thymus being invaded by lymphatic cells and thus merely became a part of a more general lymphatic affection, or whether it originated from cells in the thymus itself. With issue in the latter theory it has been discussed whether it was composed of thymocytes or developed from the lymphocytes in the thymic stroma, or directly from the epithelial supporting tissue, but all these questions will hardly be satisfactorily answered until the normal histogenesis of the thymus has been fully elucidated.

Symptoms of myasthenia gravis are not mentioned in any of the available case histories. In this connexion it must be pointed out that except for the localisation there is no demonstrable essential difference between these »thymus leukemiae» and leukoses associated with tumors of similar composition but in other sites.

If it should be found that the tumor remains localised to the thymus for some time, and only later becomes generalised, there should be a possibility for operative treatment. In this connexion it may be of interest to call attention to the experiments which have recently been made by FÜRTH and others respecting the effect of extirpation of the thymus on the development of leukosis in disposed mice; in which it was found that removal of the gland while the animals were still young lessened the frequency of later occurring leukosis. But so far roentgen treatment has proved the most effective, because these tumors are among the most

radiosensitive known. It has sometimes been advised against on the ground that it should hasten the development of the leukemic phase and, in fact, it is rather evident that the latter often sets in, or becomes more vehement, immediately after the irradiation treatment has been instituted. But there is no sure proof in the matter, and to deprecate the roentgen treatment on this ground is hardly reasonable. It often gives considerable relief to the half-suffocated patients, and finally it must be remembered that it is entirely impossible to say beforehand what cases will become generalised (STEWART-HARRISON). On the other hand there is every reason to stress the necessity of cautious dosage in the beginning.

SUMMARY

The combination of tumor in the anterior portion of the mediastinum with a leukemic blood picture is relatively frequent. Among 217 patients with leukosis treated at the Radium Center for Jutland, in Aarhus, it was found in 4 cases. The author reviews these and, under reference to 114 other cases from the literature, discusses various questions relating to the clinical picture, hematology and pathogenesis of the syndrome. It is oftenest found in children, chiefly in boys. In most cases, the mediastinal tumor seems to have been due to a tumorous proliferation of round cells in the thymus, but the histogenetic connexion between these and the various thymic elements is not yet fully elucidated. The hematology and the changes in the organs are discussed, and it is mentioned that several circumstances seem to indicate that the tumor in many cases has been primary in relation to a subsequent generalisation. Though it is doubtful if the cases of this type can rightly be considered as constituting a pathologic entity, essentially different on the one hand from leukoses, on the other from lymphosarcomas, the author thinks that there are good grounds for considering them, clinically, as a separate group. It is possible that the application of radiation therapy may in some cases hasten the development of the leukemic phase, but as palliative measure a cautious roentgen treatment is nevertheless of great value, as means of reducing the great severity of the symptoms caused by the presence of the large intrathoracic tumor, which often is extremely radiosensitive.

ZUSAMMENFASSUNG

Die Kombination eines Tumors in der vorderen Partie des Mediastinum mit einem leukämischen Blutbilde kommt verhältnismässig häufig vor. Unter 217 im Radium-Zentralkrankenhause Jütlands in Aarhus behandelten Kranken mit Leukose wurde sie 4mal gefunden. Verf. berichtet über diese Fälle und bespricht unter Erwähnung von 114 anderen Fällen aus dem Schrifttum die verschiedenen, das klinische Bild, die Hämatologie und die Pathogenese des Syndroms betreffenden Fragen. Der Zustand wird am häufigsten bei Kindern, besonders Knaben, gefunden. In der Mehrzahl der Fälle scheint der Mediastinaltumor durch eine tumorartige Wucherung von Rundzellen im Thymus bedingt gewesen zu sein, doch sind die histogenetischen Beziehungen zwischen diesen Zellen und den verschiedenen Thymuselementen noch nicht völlig klargelegt. Das Blutbild und die Veränderungen in den Organen werden besprochen, und es wird erwähnt, dass verschiedene Umstände dafür zu sprechen scheinen, dass der Tumor in vielen Fällen im Verhältnis zu einer späteren Generalisation das Primäre darstellt. Obwohl es zweife-

ıft ist, ob die Fälle von diesem Typus mit Recht als eine pathologische Einheit anzu- hen sind, die sich einerseits von den Leukosen, andrerseits von den Lymphosarkomen sentiell unterscheidet, meint Verf., dass man sie aus guten Gründen klinisch als eine sondere Gruppe betrachten kann. Es ist möglich, dass die Verwendung von Strahlen- handlung die Entwicklung der leukämischen Phase in gewissen Fällen beschleunigen nn, doch ist vorsichtige Röntgenbehandlung als palliative Massnahme immerhin von ossem Wert, als Mittel zur Verminderung der überaus schweren Symptome, die die genwart des grossen intrathorakalen Tumors, der oft äusserst strahlenempfindlich ist, rvorruft.

RÉSUMÉ

L'association d'une tumeur du médiastin antérieur avec une image sanguine de leu- mie est relativement fréquente. On l'a trouvée 4 fois chez 217 malades leucémiques traités au Centre Jutlandais du Radium à Aarhus. L'auteur relate ces 4 cas et, en se référant à 114 autres de la littérature, il discute de diverses questions touchant le tableau clinique, les caractères hématologiques et la pathogénie du syndrome. Celui-ci se rencontre le plus souvent chez des enfants, et particulièrement des garçons. Dans la plupart des cas la tumeur du médiastin semblait due à la prolifération néoplasique des cellules rondes du thymus, mais le lien histogénétique entre celles-ci et les divers éléments de la glande n'est pas encore complètement connu. L'auteur discute de l'hématologie et des altérations des organes, et il dit que certaines circonstances paraissent indiquer que dans bien des cas la tumeur a joué un rôle primordial dans la généralisation subséquente. Bien qu'il soit douteux que les cas de ce genre puissent être considérés à juste titre comme une entité pathologique différant essentiellement des leucémies d'un côté et des lymphosarcomes de l'autre, l'auteur pense qu'il y a de bonnes raisons d'en faire, cliniquement, un groupe à part. Il est possible que la radiothérapie soit susceptible de hâter dans certains cas l'apparition de la phase leucémique, mais en tant que mesure palliative un traitement prudent aux Rayons Roentgen n'en est pas moins d'une valeur considérable, car il est un moyen d'atténuer la grande sévérité des symptômes causés par la présence de la volumineuse tumeur intrathoracique, laquelle est souvent extrêmement radiosensible.

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For a fuller bibliography, the reader is referred to Cooke (70 references not listed here).

FROM THE ROENTGENOLOGICAL DEPARTMENT, CAROLINE HOSPITAL (KAROLINSKA SJUKHUSET), STOCKHOLM (HEAD: PROFESSOR ÅKE ÅKERLUND)

ON THE RADIOLOGICAL EXAMINATION OF THE EUSTACHIAN TUBE IN CASES OF CHRONIC OTITIS[1]

by

Sölve Welin

The Eustachian tube has attracted much increased interest in recent years. The rapid advance of aviation, and the consequently increased medical demands on the fitness of flying personnel have greatly contributed to this. A number of papers on this subject have been published by medical men concerned with flying, and new conceptions of diseases have been created, *e.g. aero-otitis media acuta*. This complaint is directly ascribed to the functional failure of the tube.

A study of not only this modern literature, but also older papers, shows that a number of interesting problems still remain unsolved not only as regards the healthy or diseased tube, but also as regards morbid changes in its surroundings. Little is for instance known of the variations, nature, or localization of the stenoses and strictures of the tubal canal, or of their relations to the aural diseases.

The Eustachium is primarily a regulator of the air in the middle ear. This and the outside air must be in equilibrium; the ventilation of the tube in airmen is accordingly more important. In diving, for instance, the pressure must be very quickly equalized, so that any deficient functioning of the tube canal or attendant pains may not interfere with the work of the airman concerned.

Anatomical investigations have shown that the Eustachium may vary considerably in width, and that projecting bony edges may occasionally produce a stricture of the canal to a fraction of a millimetre or cause a bend in it which, though allowing air to pass, will hardly admit a probe.

Extreme tubal strictures are, however, considered fairly rare. They are supposed to occur almost exclusively in cases complicated by other

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chronic nasal or laryngeal complaints, sinusitis, hypertrophies, septum deviations, or chronic catarrhs.

An ordinary cold will relatively often detrimentally affect the tubal passage. According to ZÖLLNER even fairly severe congestion of the vessels due to a long motor cycle trip in cold weather may impede the passage of the air.

Formerly it used to be considered that a concave ear drum always meant too low intra-tympanic pressure. Recent research has shown, however, that, unless the tubal passage has been simultaneously tested, this clinical finding does not prove that the intra-tympanic pressure is too low. The increased inward twisting of the shaft of the *malleus* may, according to ZÖLLNER, be due to morbid changes in the chain of ossicles, and the *convex* bulge of the ear drum to a loss of pressure by a degeneration of the *membrana propria* with consequent loss of normal vaulting and elasticity.

The diminution of the patient's various symptoms — ache, buzzing in the ears, and dizziness — and the improvement of the hearing when air is blown in *ad mod. Politzer*, used to be interpreted as a criterion of tubal stricture, but recent research has proved this opinion to be occasionally faulty, as the improvement may also be due to other causes than the removal of under-pressure.

The diagnosis of under-pressure may thus be difficult, but according to ZÖLLNER it is in addition definitely proved that the tube may be stopped up for a whole day without any resulting troubles — no ache, normal tympanum, and normal hearing — and producing subjective symptoms only in the event of extreme variations of pressure.

As has already been mentioned above, there is general agreement that the anatomical width of the tubal canal is important, and clinicians have attempted to determine this by various means. As their methods do not allow any exact mapping, however, radiology has been resorted to.

The first attempts were made by PORTMAN, RETROUVEY and LECHAPÈLE. Their investigations were made on corpses using amalgam as a contrast medium, as they assumed that iodized oil would give too little contrast. They described the normal anatomy, and proved that the isthmus was situated on the boundary between the cartilaginous and osseous parts.

The first to examine living people radiologically were REVERCHON and WORMS. In a paper published in 1925 they pointed out that this radiological examination had always been considered very difficult to perform on living people on account of the shape of the tube, which had prevented its being filled with contrast medium. They themselves had managed to fill it with lipiodol without causing any pain to the patients, who were all suffering from otitis with large perforations of the ear drum.

They injected the contrast medium from the pharynx, and obtained beautiful pictures of the tube which clearly showed the oblique course of the tube from the middle ear to the pharynx and also allowed them to determine the width and strictures of the tube.

SPIELBERG, who published his results two years later — in 1927 —, had inserted silver catheters in the tubes and afterwards dropped lipiodol into these. He, too, had in this way been able to demonstrate the course, length, and width of the tubes, and found that the width varied from 2 to 3 mm in the bony part, and from 1 to 1.5 mm in the cartilaginous part.

In 1938 HEIMENDINGER gave an account of his experiences with a flexible catheter. He had examined projections from the front as well as in profile, and had also used axial pictures taken submento-vertically. He stated that his method enabled him to show the shape and permeability of the tubal canal as well as the exact position of any obstruction.

In an article published in 1941 REES-JONES and MCGIBBON reported their results of Roentgen examinations of the Eustachian tubes of 34 patients treated for deafness in one of the Royal Air Force hospitals. In these cases the deafness was connected with inadequate ventilation of the tube and was assumed to be primarily due to an obstruction in the tube with consequent inequality of the atmospheric and intratympanic pressures.

In all these cases they had also after injection of a contrast medium been able to demonstrate an obstacle, the extent and nature of which, however, they were unable to decide.

These authors pointed out the fundamental importance of using a non-irritant contrast medium of low viscosity and of avoiding superimposed bone shadows. In some cases the patients had felt a sharp aural pain for a few seconds, but they did not regard this as a sign of an open tube, since it had occurred in cases of tubal obstruction.

According as the obstruction was situated close to the *ostium pharyngeum* or in the vicinity of the *isthmus* the changes revealed by the Roentgen picture varied in character. In the former case a slowly narrowing contrast shadow with relatively smooth edges was obtained, while in the latter case pooling of the opaque medium gave rise to appearances which were typical »mushroom-like» shadows.

In the Caroline Hospital, too, we have for some years been examining the Eustachian tube radiologically, and our material now comprises 30 cases. All these have been cases of *otitis* with more or less reduced hearing, of tumours in the neighbourhood of the Eustachian tube, or finally also of slight deafness. In several of them we have been able to record interesting findings and to demonstrate the anatomical basis of some of the symptoms which has been impossible to do with certainty by any other method of examination.

Like SPIELBERG, we have used fully axial pictures with submento-vertically directed rays, but have also employed the symmetrical parieto-occipital projection, proposed — independently of one another — by ALTSCHUL and by WORMS and BRETTON, whereby both the mastoid processes are pictured by semi-axial rays. In our experience pictures in these two projections supplement one another excellently, and both of them project the two Eustachian tubes free along their full length. In purely profile pictures the tube will be so shortened that I have ceased to use that projection.

In most cases we used iodized oils, 10 and 40 % iodipin, as a contrast medium, but a satisfactory density can also be obtained with the water-soluble 35 and 50 % contrast media.

In patients whose ear drums were perforated the contrast medium was injected through the outer auditory canal, using a pressure syringe designed by Dr N. WASTENSSON to close the outer canal effectively and exposing the film while injecting the contrast medium.

In a few cases whose ear drums were intact the contrast medium was injected through the *ostium pharyngeum tubae auditivae*. It was then at first difficult to avoid leakage; in order to close the opening of the tube effectively we had therefore to construct cone-shaped plugs of ordinary or vulcanized rubber; the latter were made from actual casts of the tube opening and its immediate surroundings in corpses.

In this manner we could also fill the tube almost to its full length from the pharynx, but in view of the risk of infection we dared not exert sufficient pressure to make the contrast medium penetrate right into the tympanum.

It is worth noting that these examinations as a rule did not inconvenience the patients at all. Only two of all our cases said they felt pain during the examination. In both of them the examination was stopped, and the deficient filling of the tube in these cases can therefore not be regarded as evidence of a certainly obstructed passage.

No signs of irritation could ever be objectively demonstrated, although in 22 cases the contrast medium had passed through the *aditus ad antrum* up into the antrum and more or less far into the peripheral cell system of the mastoid process.

The analyses of the pictures showed that no findings can be definitely regarded as pathologically significant unless the same change can be demonstrated in the radiograms taken in both directions.

In our opinion, which so far unfortunately does not rest on any pathologically or anatomically verified grounds, conditions were normal in 18 of our cases, and in these we have recorded smoothly and distinctly outlined, straight tubes, slightly widened towards both the pharynx and the middle ear. As a rule it has been possible to fix the boundary between

Fig. 1.

Fig. 2.

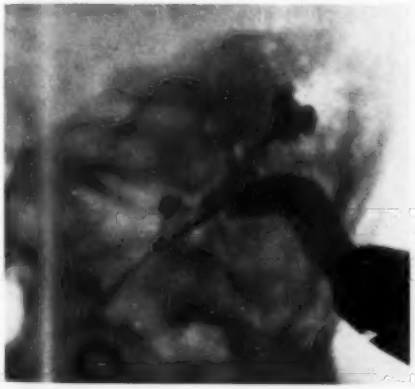

Fig. 3.

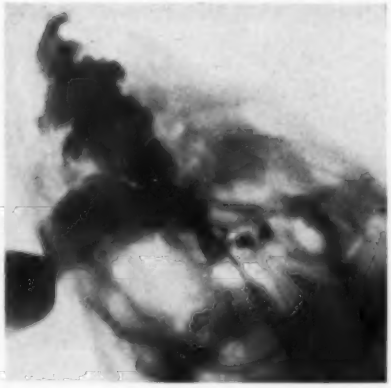

Fig. 4.

Fig. 1. Normal picture, semi-axial projection.
Fig. 2. Fully axial projection of the same case.
Fig. 3. Racemose groups of contrast-filled peritubal air-cells.
Fig. 4. A more elongated group of contrast-filled peritubal air-cells.

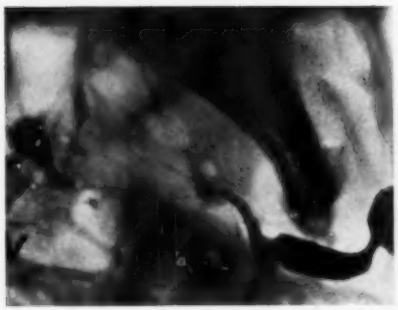

Fig. 5.

Fig. 6.

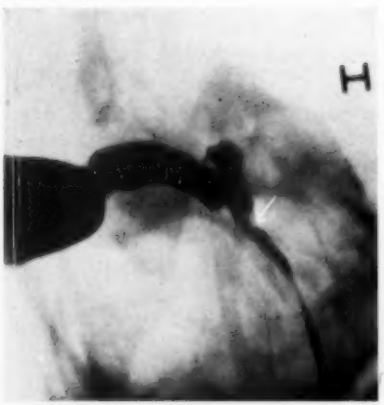

Fig. 7.

Fig. 8.

Fig. 5. Anatomical anomaly in the form of a crescentic tube in a case of clinically demonstrated tubal stenosis.

Fig. 6. Local stricture at the isthmus.

Fig. 7. Polyp-shaped defect in the osseous part of the tube. No clinical signs of stenosis.

Fig. 8. Inflammatory changes in the entire tubal mucous membrane in a patient with clinical inflammatory changes round the tubal orifice.

Fig. 9.

Fig. 10.

Fig. 9. Fully axial projection of the same patient.

Fig. 10. Stenosis at the transition between the tympanum and tube in a case of clinical tubal stenosis.

the tympanum and the tube fairly exactly, and the osseous portion of the tube was generally slowly tapered. Figs. 1 and 2 are from normal material.

In 6 cases peritubal air-cells had filled, and fig. 3 indicates a racemose grouping of air-cells near the isthmus, while fig. 4 shows an elongated bunch of air-cells connected with the lateral part of the tube and continuing in towards the apex of the pyramid.

In 10 cases deflections from what we consider normal were demonstrated. Fig. 5, for instance, shows a peculiar course of the tube. We have interpreted this as an anatomical anomaly, which in all probability affords a sufficient explanation of the obstructed passage through the tube recorded in the clinical examination.

Local strictures at the isthmus — fig. 6 shows one such — were observed in two cases, and in two others a diffuse stricture of the full length of the tube. When injecting the two latter cases we had a feeling that it was more difficult to press in the contrast medium, but no certain diagnosis was possible until the changes had been studied in the radiograms. In all four cases the contours of the tube were distinct.

Polyps, or perhaps more correctly polyp-like defects, were twice disclosed by the contrast, in both cases localized to the bony part of the tube. Fig. 7 is one of these.

In two cases the whole contour of the tube was irregular and slightly ragged, and these changes were interpreted as inflammatory — fig. 8 and 9. In one of them the clinical examination disclosed inflammatory changes at the tubal orifice, which may be deemed to confirm our opinion to some extent. In a third case — fig. 10 — we finally found a very abrupt transition from the tympanum to the tube, the latter being in addition strongly constricted and of slightly irregular contour. This, too, was assumed to be due to some inflammatory change in the mucous membrane.

New, possibly malignant, growths were also looked for in some patients, but so far we have not found any such. We have not yet succeeded in injecting any contrast medium into the tubes of cases where tumourous masses had been clinically demonstrated round the *ostium pharyngeum tubae auditivae*. There seems to be no reason, however, why this method should not render a diagnosis possible in the early stages of such growths. If it is correct that some epipharyngeal tumours emanate from the Eustachian tube, it should then be possible to make an earlier diagnosis by this than by any other method of examination.

SUMMARY

The author has filled the Eustachian tube with contrast medium in 30 cases of chronic otitis and examined pictures in two projections: a) a fully axial picture taken with submento-vertically directed rays, and b) a semi-axial picture taken with parieto-occipitally directed rays. In 9 cases he succeeded in demonstrating pathological changes such as strictures, polyps, or inflammatory changes in the mucous membrane, thus securing anatomical explanations of the clinical findings.

ZUSAMMENFASSUNG

Verf. hat bei 30 Fällen von chronischer Otitis die Tuba Eustachii mit Kontrastmittel gefüllt und in zwei Projektionen gemachte Aufnahmen untersucht: 1. Ein völlig axial aufgenommenes Bild mit submento-vertikaler Strahlenrichtung und 2. eine semi-axiale Aufnahme mit parieto-occipitaler Strahlenrichtung. In 9 Fällen gelang es ihm, pathologische Veränderungen, wie Strikturen, Polypen oder entzündliche Veränderungen der Schleimhaut, darzustellen, wodurch die klinischen Befunde ihre anatomische Erklärung bekamen.

RÉSUMÉ

L'auteur a rempli de substance opaque la trompe d'Eustache dans 30 cas d'otite chronique et examiné les images prises dans deux projections: a) l'une complètement axiale, avec rayon central vertical partant de la région submento-verticale, et b) l'autre semi-axiale, avec rayon central pariéto-occipital. Dans 9 cas il a réussi à mettre en évidence des lésions pathologiques telles que sténoses, polypes, ou des altérations inflammatoires de la muqueuse, obtenant ainsi une explication anatomique des constatations cliniques.

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